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HOLLAND: BIRTH INJURY IN RELATION TO LABOR

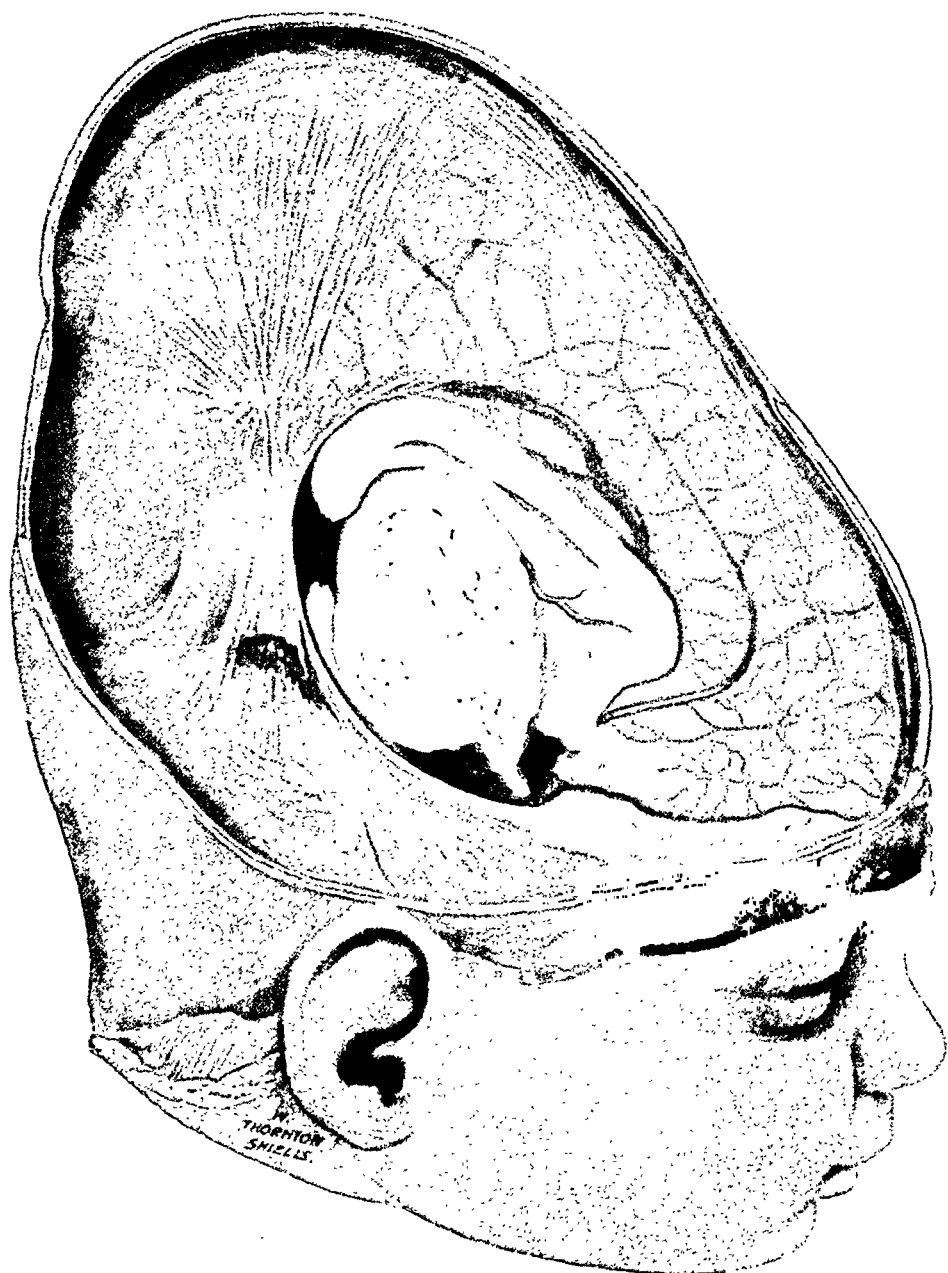


Fig. 1.—(Case 78.) Incomplete tear of tentorium cerebelli on right side; the tear is across the fibers at the base of the anterior vertical band. The head shows extreme molding after labor with generally contracted pelvis. Note elevation of apex of tentorium and change in direction of vein of Galen and straight sinus. (From Elden and Holland: Midwifery.)

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Original Communications

BIRTH INJURY IN RELATION TO LABOR*

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THE VULNERABILITY OF THE FETUS TO BIRTH INJURY

THE human fetus is peculiarly liable to injury during birth. Even at the term of pregnancy it is relatively immature and runs far greater risks than the more robust young of other mammals. None of its tissues—bones, epiphyses, muscles, viscera, or blood vessels—are well adapted to withstand the application of force; and, above all, its thin, plastic and incompletely closed cranium gives very poor protection.

Even under the best possible birth conditions injuries are liable to occur. The conditions, however, are by no means always favorable, and it is believed that they are in some respects becoming less so. Nowadays there are factors, increasingly common, which may act prejudicially; such, for example, as elderly primiparity, the demand for shorter and more comfortable labors, the over-use of anesthetic and oxytocic drugs, and the abuse of the obstetric forceps and labor induction. The wonder surely is not how many babies are injured but how many are born intact.

As regards causation one may make the general statement that the problem is a mechanical one, a consideration of the stresses of labor and the varieties of strain they may produce on the body of the fetus. Besides the immediate mechanical factor, two important predisposing factors must be emphasized, prematurity and asphyxia. The increased liability of the premature fetus is obvious. The effect of asphyxia will

*Read (by invitation) at the Sixty-First Annual Meeting of the American Gynecological Society, Absecon, N. J., May 25 to 27, 1936.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

be discussed more fully under intracranial injuries; here it will merely be pointed out that an engorged vessel will rupture more easily and will bleed more.

A list of injuries would include almost every organ and tissue of the body; some are mortal, some merely crippling, but the vast majority are without any effect, immediate or remote. Philip Schwartz states that some traumatic effect of labor on the brain can be demonstrated in 90 per cent of all newborn and young infants coming to autopsy, and Ehrenfest's proposal that we must distinguish between "physiologic" and "pathologic" trauma is most illuminating in this respect.

THE EFFECT OF BIRTH INJURY ON INFANT LIFE AND HEALTH

To appreciate the scope of our problem we must study its effects in three directions: namely (1) stillbirth, (2) infant mortality in the early weeks of life, and (3) natal morbidity, i.e., permanent mental or physical crippling. We have two sources of information, national statistics as published by Departments of Health, and the results of special investigation into large series of cases. National statistics do not help much as regards the effect of birth injuries on the stillbirth rate. They merely state the rate. In England and Wales the registration of stillbirths did not become operative until the year 1928, since when the annual rate has averaged about 40 per 1,000 live births. No attempt is made to classify them into cases of antenatal and cases of intranatal death (i.e., into macerated and fresh fetuses), or to demand the cause of death, in the certificates. Indeed this would be impossible; for every case would require at least an expert autopsy. However, we can get a rough idea of the toll which birth injury takes on infant life from the results of investigations into large series of cases; most workers agree that about one-half of all cases of intranatal death reveal evidence of birth injury.

As regards infant mortality national statistics give valuable information. They reveal that, although the infant mortality for the first year of life has fallen in a remarkable manner during the last twenty-five years, there has been relatively little fall during the early days of life. We, as obstetricians, can claim hardly any share in this triumph of preventive medicine. The causes of death during the first four weeks of life are preponderatingly obstetric, namely, birth injury, prematurity, and septic infections, each accounting roughly for about one-third of the deaths.

Table I shows the age distribution of infant mortality rates between 1906 and 1930 in England and Wales. The figures reveal that when the two quinquennia 1906 to 1910 and 1926 to 1930 are compared, (a) the deaths under one year fell by 42 per cent, (b) the deaths under four weeks fell by only 20 per cent, and (c) the deaths under one week fell by the comparatively small figure of 9 per cent.

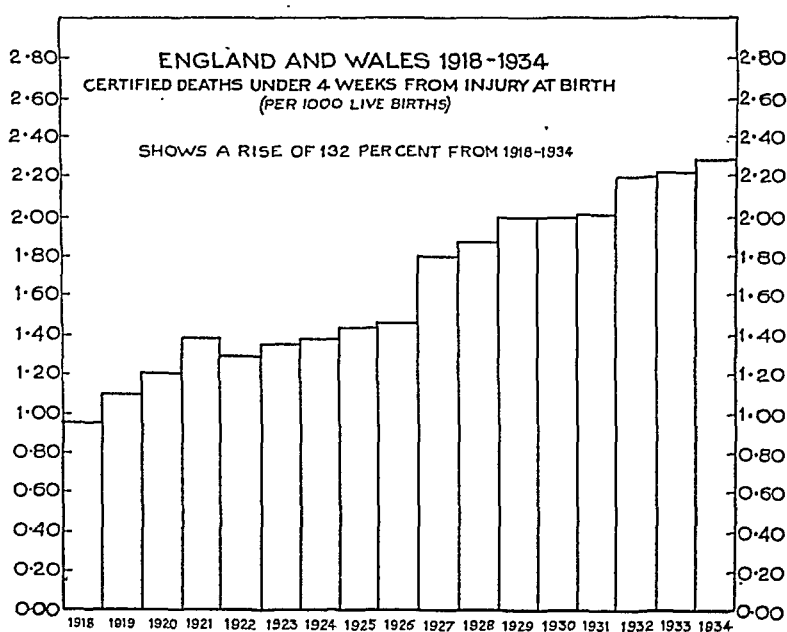
TABLE I. AGE DISTRIBUTION OF INFANT MORTALITY, 1906-1930, IN ENGLAND AND WALES (RATES PER 1,000 LIVE BIRTHS)

YEARS	DEATHS			
	UNDER ONE DAY	UNDER ONE WEEK	UNDER FOUR WEEKS	UNDER ONE YEAR
1906-1910	11.5	24.5	40.2	117
1911-1915	11.4	24.1	39.0	109
1916-1920	11.0	23.4	37.0	91
1921-1925	10.4	21.7	33.4	75
1926-1930	10.3	21.8	31.8	68

IS THE DEATH RATE FROM BIRTH INJURIES RISING?

If we misread our national statistics, we may be led to believe that deaths from birth injuries are increasing in number and to draw false inferences therefrom.

TABLE II



L. K. Frankel, a vice-president of the Metropolitan Life Insurance Company, New York, dealing in 1927 with the infant mortality figures in the United States registration area, drew attention to what he called "the startling fact" of the sharp increase in the death rate from birth injuries, and inferred that it was due to the increased use of instruments to hasten delivery. If we examine the figures for England and Wales, as shown in Table II, we see a progressive rise from 0.98 per 1,000 in 1918 to 2.27 per 1,000 in 1934, an increase of 132 per cent. Are we therefore justified in asserting that the number of deaths from birth injury has increased in this remarkable manner? By no means. All we can infer is that the number of deaths *certified by doctors* as due to birth injury has increased. During the last twenty years knowledge about birth injuries and their diagnosis has become widely diffused, and

death certification in this respect must have vastly improved. The injuries are not more in the heads of the babies, but more in the minds of the doctors.

THE VARIETIES OF BIRTH INJURY

A complete list of injuries would have to include every tissue and organ in the body, and I do not propose to make one. Intracranial injuries are the commonest and they present the most important problems as regards production, prevention, diagnosis, and treatment. My classification will therefore be a simple one: I. Other injuries, and II. intracranial injuries.

I. INJURIES OTHER THAN INTRACRANIAL

A brief mention of the most important must suffice: (1) skin and subcutaneous tissues anywhere, but chiefly the scalp, (2) muscles (sternomastoid), (3) fractures of bones: skull, clavicle, humerus, and femur, in order of frequency, (4) separation of epiphyses, (5) rupture of, or hemorrhage into abdominal viscera (liver, suprarenal), (6) damage to thoracic viscera (rare), (7) peripheral nerve injuries (facial, brachial), (8) the eye, direct injury or hemorrhage, (9) injuries to spinal cord and vertebral column.

Damage to the spinal cord is a commoner cause of fetal and neonatal death than is generally supposed and may occur during the forcible extraction of the aftercoming head or of large shoulders in head presentation. It is often overlooked at autopsy. Rupture of the liver is a not uncommon mortal injury inflicted during difficult breech delivery and is due to clutching the fetus by the abdomen.

II. INTRACRANIAL INJURIES

Considering the peculiar liability of the head to injury, it seems on first thought strange that it should act as the battering-ram by which the fetus forces its way into the world. Nevertheless, when the head comes first it is far less liable to injury than when it comes last. It is apparent that the inherent disabilities of the head, considered as a body exposed to stress, are to a certain extent compensated by certain protective properties. Its plasticity enables it to undergo changes in shape which adapt it to the changing shape and direction of the birth canal; its elasticity enables it to regain its shape in the intervals of stress, and so to place the intracranial contents again in a state of rest; its capacity, to a certain extent, to expand allows it to gain a little respite from the swelling of intracranial congestion and edema; and the arrangement of dural septa acts as stays or ligaments, which tend to restrain a dangerous degree of distortion.

In practical obstetrics the study of the head as a birth object is of great interest and importance, for the obstetrician who understands the mechanical problems involved will injure fewer heads than he who

does not. During its passage the head is in a state of compound compressive stress, the resultant between the powers of labor and the resistance of the maternal passages. This stress may be roughly regarded as consisting of two elements: (1) a general compression of the whole head, (2) a simple longitudinal compression by opposite forces acting at the ends of the diameters of engagement, i.e., the diameters lying between the occiput and the forehead, and the biparietal diameter, in vertex and breech presentations. For practical purposes it may be said that the stresses and their effects vary chiefly with (1) the absolute amount of the forces acting on the head at any given time, (2) the direction in which these forces act on different parts of the head, (3) the degree of plasticity of the head, (4) whether the forces attain their maximum effect suddenly or gradually, and (5) the length of time they act.

Cranial stress may be normal or excessive. The effect of stress is strain (strains being analyzable into stretches and slides or shearing strains). Normal stress leaves no observable effect on the head or only a moderate amount of molding. Excessive stress may result in (1) excessive alteration in the shape of the head (an example of shearing strain), (2) overstretching and tearing of the dura mater septa and rupture of certain blood vessels, (3) a rise in intracranial pressure sufficient to obstruct the venous sinuses and cerebral veins and to produce cerebral congestion and edema.

The following intracranial injuries may occur:

A. Injuries to the dura mater septa (tearing of the tentorium cerebelli and falx cerebri), nearly always accompanied by one or more of the varieties of hemorrhage under Group B.

B. Injuries to blood vessels, resulting in (1) subdural hemorrhage, usually gross, from cerebral veins and dural sinuses, and associated with tearing of the dural septa, (2) meningeal capillary oozing, usually of asphyxial origin, (3) ventricular hemorrhage, from choroid plexus, (4) intracerebral hemorrhage.

C. Other effects of cerebral compression: congestion and edema of brain and meninges with increased intracranial pressure, leading to asphyxia of the brain and medullary centers.

A. *Overstretching and Tearing of the Dural Septa.*—Alterations in the tension of the septa accompany alterations in the shape of the head. This is inevitable from the nature of the attachment of the septa to the cranial bones, as can be demonstrated on a fetal head by reflecting the scalp and removing sufficient of one parietal bone to allow the cerebral hemisphere to be removed and the septa to be viewed from that side (Fig. 1, frontispiece). On compressing the head in the suboccipitobregmatic diameter, the head becomes shortened anteroposteriorly by forward displacement of the occipital bone and heightened vertically by bending and elevation of the vault (Fig. 1). If at the same time the septa are observed, the middle two-thirds of the falx cerebri and the tentorium will be noticed to become stretched and tense. Moreover, the septa move as a whole, as will be appreciated by observing the anterior point of junction between the falx and tentorium (the site of entrance of the vein of Galen into the straight sinus) which becomes displaced upward and forward, the forward movement being much the more pronounced. If now by stronger compression the tension is increased, the tentorium tears near its free border just below its junction with the falx (Fig. 1).

It is seen that bending of the bones and excursion of the vault is resisted by the septa and when the septa tear a restraining influence is removed. The septa may be regarded as exerting a protective function in labor, forming a defensive system against excessive alteration in the shape of the head. Reasonable molding of the head is beneficial; but undue distortion may jeopardize the life of the fetus by producing intracranial disturbances, the most important of which is hemorrhage from the overstretching and rupture of certain blood vessels.

The view that the septa are designed to take stress is supported by the fact that they contain strengthening bands and fibers arranged on admirable mechanical principles along the lines where stress is most likely to fall. These bands are, in my opinion, developed in order to enable the cranium and its contents to withstand the effects of excessive stress during labor. An anteroposterior and a vertical

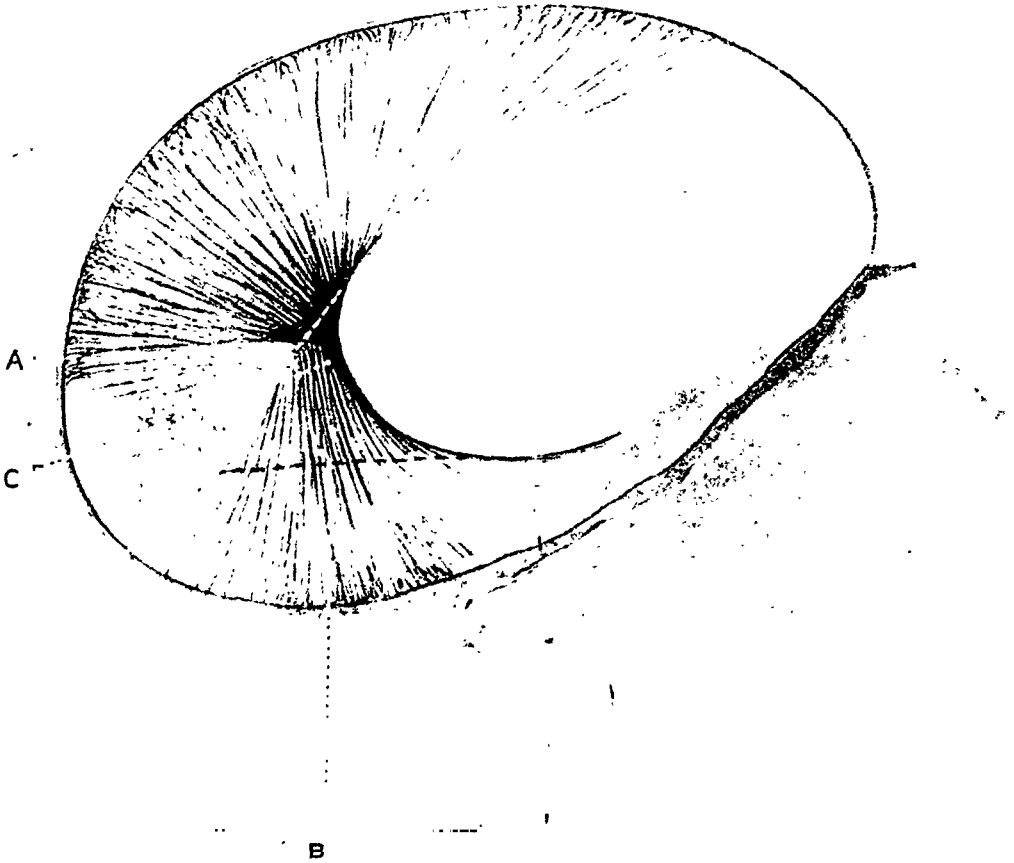


Fig. 2.—Semidiagrammatic drawing to show arrangement of fibers in falx and in superficial layer of tentorium, after removal of parietal and part of occipital and frontal bones. *A*, points to black dotted line indicating floor of straight sinus; *B*, points to white dotted line indicating position of deep horizontal band; *C*, points to anterior vertical band.

system may be described. It is to the latter (Fig. 2) that I wish particularly to draw attention, for it is a beautiful example of the mechanical system of stress-lines. It consists of two opposing sets of convergent fibers which meet in their points of convergence. From above downward converge fibers from the middle two-thirds of the falx, and from below upward converge fibers from the tentorium. They meet in a strong band which I call the anterior vertical band of the tentorium. This band is subjected to stress in almost every labor and is the usual site of tentorial tears.

Tears of the tentorium and falx, as found in dead fetuses, support this theory of cranial stress. Tentorial tears are nearly always situated in what has been

described as the area of greatest stress, just below the junction with the falx anteriorly (and implicating the anterior vertical band). Tears of the falx cerebri are found relatively infrequently; they usually occupy the middle two-thirds and are elliptical, with the long axis of the ellipse lying, as would be expected, in the line of greatest stress (Fig. 3). The tears may affect one or both sides of the tentorium and may be complete or incomplete. Incomplete tears involve only the superficial layer. Complete tears usually involve the free border of the tentorium, but sometimes the free border is left intact and the tear appears as a perforation. Very commonly a small hematoma is found in the region of the tentorium which commonly tears; this is probably an effect of excessive stretching without tearing. Tears of the dural septa are not in themselves to be regarded as fatal injuries;

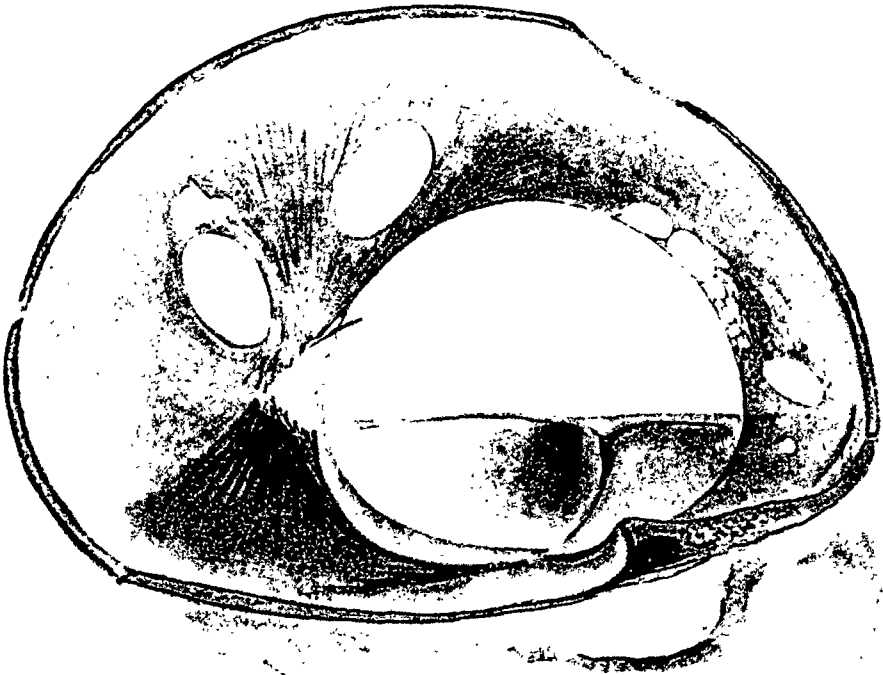


Fig. 3.—Complete tear of tentorium cerebelli, elliptical tears of falx cerebri. The tear is in the right side of the tentorium. The anterior one-third of the line of junction between the tentorium and falx has been torn through. The straight sinus (indicated by bristle) has been opened.

they bleed very little and sometimes not at all. They are the expression of excessive intracranial stress, the mortal lesion being the accompanying intracranial effects, namely cerebral hemorrhage and the asphyxial effects of intracranial pressure.

B. Injuries to Blood Vessels.—Etiologically there are two varieties of intracranial hemorrhage, traumatic and asphyxial. Gross hemorrhage is probably always traumatic; it occupies the subdural space and is nearly always found associated with tears of the dural septa. But asphyxial venous engorgement is a most important contributory factor in traumatic hemorrhage, for engorged veins rupture more easily and bleed more freely. Clear postmortem evidence of fetal asphyxia is usually found in cases of gross hemorrhage. A clear differentiation between traumatic and asphyxial bleedings is not always possible, and they often occur together. Engorge-

ment of the cerebral veins may be part of a general asphyxia, or may be a local affair due to obstruction of the cerebral veins from cerebral compression ("traumatic cerebral asphyxia"—see below).

Only when large vessels have ruptured is it possible to track down the hemorrhage to its source. Large veins commonly found ruptured are the vein of Galen and the cerebral veins entering the superior longitudinal sinus. Sometimes the venous sinuses themselves are opened; most commonly, as would be expected, the straight sinus, more rarely the superior longitudinal and lateral sinuses. I was able to detect rupture of the vein of Galen in only two of my cases; but A. C. Palmer, whose observations in a series of cases of cerebral hemorrhage were exceptionally complete and careful, found evidence of rupture of this vein in eight out of nine cases of subdural hemorrhage with laceration of the tentorium and falx cerebri. Reference to Fig. 1 shows the mechanism by which this important vein or its tributaries are ruptured. Any movement of the apex of the tentorium is necessarily transmitted to the vein of Galen whose upper fixed point is at its entrance into the straight sinus. It has already been pointed out that in the common form of head distortion the apex of the tentorium is drawn upward and forward. The vein follows this displacement with the result that it is stretched and has its line of direction so altered that it gets kinked and obstructed at its entrance into the sinus. Great engorgement of the vein is a striking appearance in most cases of intracranial injury.

The site as well as the size of a hemorrhage is of importance as regards its effect; large hemorrhages kill by cerebral compression and damage to the respiratory centers; hemorrhage in the posterior fossa (infratentorial hemorrhage) is more damaging than elsewhere in the subdural space.

C. Hemorrhages in the Brain Substance.—The concentration of interest on septal and vascular injuries led workers to overlook pathology of the brain itself. But in 1924 P. Schwartz began to publish work of outstanding importance. He removed the brain intact, studied it histologically and found petechial hemorrhages and small areas of necrosis in a remarkably high proportion of newborn children. The hemorrhages were definitely related to the distribution of the tributaries of the vein of Galen (*vena terminalis*, *vena lateralis ventriculi*, *vena choroidea*), and the necrotic areas appeared as opaque yellowish spots, often in confluent groups, in the central white matter and basal ganglia around the third and lateral ventricles. Schwartz makes the remarkable pronouncement that micro- or macroscopic hemorrhages or their sequels can be found in the brains of approximately 95 per cent of infants dying in the early weeks of life. He failed to find any of these appearances in the brains of a control series of brains of newborn animals with thick cranial bones and no fontanels, and points out the lack of protection afforded by the peculiarly thin and plastic cranium of the human fetus.

Schwartz's work has given rise to a good deal of controversy. Cruickshank points out the technical difficulties which arise in the preparation of the brains of the newborn for histologic examination; the soft and watery brain tissues are easily damaged during removal, undergo rapid autolyses, and shrink badly during fixation and embedding. A case reported by Kirkwood and Myers shows the importance of making a complete examination of the brain. After an easy normal labor an infant developed attacks of apnea and cyanosis and died twelve hours after birth. At autopsy no macroscopic intracranial damage was found, but serial sections through the brain stem revealed small hemorrhages in the lower part of the pons.

D. Other Effects of Cranial Compression.—Prolonged cranial compression may obstruct the venous sinuses and cerebral veins and produce asphyxia of the brain and medulla. The autopsy lesions are intense congestion and edema of the brain and meninges, and this still further increases the intracranial pressure. This condition is sometimes classed under "intracranial lesions without hemorrhage," but I prefer to call it "traumatic cerebral asphyxia." The effect of asphyxia of the

respiratory center would be to stimulate it, and the fetus would make intrauterine respiratory efforts, the presence of amniotic fluid in the trachea or bronchi in some cases of stillbirth being evidence of such efforts. The alteration in the intrathoracic pressure as the result of the inspiratory efforts would lead to venous obstruction in the heart and great vessels and an intense engorgement of the whole venous system, i.e., to the phenomena of generalized asphyxia. Such asphyxia would not necessarily be fatal; if prolonged it would lead to increasing paralysis of the respiratory center, causing the center to fail to respond to stimuli following delivery. Cruickshank lays special emphasis on increased intracranial pressure as a factor of the first importance in the production of a large proportion of cases of neonatal death.

STILLBIRTH: RELATION OF THE TYPE OF LABOR TO INTRACRANIAL INJURIES

In presenting this aspect of the subject I shall use my own original material, the results from which show no essential differences from those obtained by other workers. The main issue is, in what sort of cases is intracranial injury especially liable to occur, taking injury of the dural septa as the chief criterion?

There were 167 fresh fetuses (consecutive cases of intranatal fetal death) and tentorial tears were found in 48 per cent. There were 46 cases of head presentation, and 35 cases of breech presentation. The preponderance of breech presentations is remarkable, and shows the great liability to intracranial injury in breech labor.

Of the head presentations 44 were vertex, and one is at once struck by the high proportion of cases in which the forceps was used, 25 out of the 44 cases. Doubtless a certain number of the forceps extractions were for "disproportion" but all were "low forceps" except five. The occurrence of tentorial tears after a low forceps operation invites criticism. The use of the forceps is one of the central problems connected with the production of intracranial injury, as well as with its prophylaxis, as will be discussed later.

Another point which attracts notice is that the injuries occurred in a certain number of cases of spontaneous delivery. For some of these there was a sufficient explanation; in 37 per cent the fetus was premature and other factors were precipitate labor, the use of pituitrin and a former extensive perineal plastic operation. Nevertheless there remain a few cases in which labor was apparently in all respects normal. We should not allow these few to perturb us too much; they are rare, and it may be wiser to accept them as a natural hazard of labor, especially a first labor, rather than attempt to prevent them by a wide use of the "prophylactic forceps operation."

There were 47 cases of breech labor and tentorial tears were found in no less than 75 per cent. When the breech cases are divided into the three classes of normal breech labor (i.e., cases with no complication other than those natural to breech labor—extended arms and legs), complicated breech labor (e.g., with contracted pelvis, placenta previa), and breech by version, we see that tears were found in 88 per cent of

the cases of normal breech labor and 71 per cent of the fetuses delivered by version and extraction. Five of the normal breech babies were premature. These findings are common knowledge to us, but they are by no means yet common knowledge to the general body of doctors attending women in childbirth. They were not widely known even among obstetric experts twenty years ago, and I shall not forget the great joy that the almost constant discovery of these injuries gave me, for I felt that the mortality from breech labor could be reduced remarkably. The traditional teaching was that the great danger came when the child was so far born that the cord was compressed, and that the rest of the delivery must be hastened in order to save death from asphyxia. In consequence, it was the custom to hasten the delivery of the head and get it out within a few seconds of the birth of the trunk. The head was thereby subjected to a rapid compression in the suboccipitofrontal diameters, by being dragged forcibly through a vaginal orifice and past a perineum which were unprepared for its passage. We know now that far more breech babies are killed by head compression than by cord compression, and practice has been modified accordingly.

We may generalize as follows: Dangerous cranial stress and the resulting injury are especially liable to occur in (1) breech labor, (2) forceps delivery, (3) premature labor, (4) too rapid delivery (i.e., precipitate labor, use of oxytocic drugs), (5) states in which the cerebral vessels are congested, i.e., impending or early fetal asphyxia, clinically called "fetal distress."

PROPHYLAXIS

I begin by telling my students that they cannot expect to become good obstetricians unless they perform or assist in performing autopsies on cases of stillbirth or neonatal death; for that is the only way to learn how fragile the fetal tissues are, and how easily injuries, especially intracranial injuries, occur. I then utter the platitude that a large proportion of injuries are avoidable by good and sound obstetric practice, and the moral by showing Table III.

TABLE III. CORRELATION OF MATERNAL, FETAL, AND NEONATAL MORTALITY RATES IN ENGLAND AND WALES, 1930-1934

AREA	MATERNAL DEATHS PER 1,000 LIVE BIRTHS	STILL- BIRTHS PER 1,000 TOTAL BIRTHS	INFANT DEATHS PER 1,000 LIVE BIRTHS		
			UNDER 1 DAY	UNDER 1 WEEK	UNDER 4 WEEKS
England and Wales	4.4	41	11	22	32
County of London	3.3	32	10	18	25
Buckinghamshire	4.0	31	10	19	26
West Ham	2.6	33	9	18	25
Wales	6.1	55	12	26	37
Halifax	8.0	50	12	29	42
Oldham	7.5	55	13	29	42
Glamorganshire	6.3	58	13	27	41
Merthyr Tidal	5.8	69	11	27	40

In Great Britain there are certain areas (towns, counties, boroughs, etc.) known as "black areas" because of their high maternal mortality rate. Recently an investigation (Oxley, Phillips and Young) into the maternal deaths during the years 1929 to 1931 in one of these areas was published, an industrial town with a maternal mortality rate of 10 per 1,000. All circumstances were passed under review: social conditions, doctors, midwives, hospitals, and it came out clearly that the high death rate was due to too frequent intervention in the course of labor by the doctors. In Table III is shown the correlation of maternal fetal and neonatal mortality rates in certain areas (some "black" and some "white," for contrast) in England and Wales for the years 1930 to 1934. It is clear that a low maternal rate goes with a low stillbirth and neonatal rate, and vice versa. The inference is clear. That which caused the maternal deaths caused also the fetal and infant deaths, namely, too frequent intervention in the course of labor.

Coming now to specific points in prophylaxis, certain things stand out for consideration, bearing in mind that although the determining factor in injury is a mechanical one the two great contributory factors are prematurity and asphyxia.

In the use of the forceps there are some elementary considerations to be disposed of. Can the force exerted by the forceps ever be made to act as favorably on the head as the natural forces? To approach this ideal as closely as possible certain principles must be observed: (1) The delivery of the head must be made slowly and gradually. Most operators, even experts, extract far too quickly. (2) The tractions must be intermittent and of short duration in order to avoid continuous compression and to allow the intracranial vascular system to return to a condition of rest. (3) To ensure that as small an object as possible is presented to the maternal passages, by correcting as far as possible faulty attitude and position of the head (i.e., manual rotation of an occipitoposterior position). (4) The varying curve and direction of the birth canal must be followed. A common fault is to begin extending the head before the occiput has cleared the pubic arch. (5) It is generally advisable to reduce the resistance by episiotomy or by "ironing out" the vagina and orifice. (6) The forceps must be applied accurately to the sides of the head, for if they are applied in the occipitofrontal range of diameters they will exert compression in a direction it is particularly important to avoid.

These principles are naturally followed by experts, and in their hands it may truthfully be said that the low operation is virtually without risk. But only a fraction of forceps operations is performed by experts, and the question arises as to whether the types of instrument could not be improved to render them safer in the hands of practitioners who are not specialists. The ordinary long curved forceps and the axis traction forceps were designed to aid delivery of the head obstructed in the

midpelvis or higher. The necessity for the performance of this operation seldom arises in these days of prenatal care. Yet in the medical schools students are taught the use of a heavy and powerful instrument that can be applied to the undescended head or when the os is not fully dilated. (We are all familiar with the tragedy of the "failed forceps.") Is this wise? Would not an immense amount of injury be avoided if students were taught the use of an instrument that could be used only when the head is low in the pelvis? Such an instrument has been designed by Wrigley and has much to recommend it. It is the Simpson short straight forceps to which the usual pelvic curve has been added to the blades. It is very lightly made (being only about one-fourth the weight of the ordinary long curved forceps), and its construction is such that it is impossible to exert a tremendous pull, so that the risk of head injuries should be greatly lessened.

An important problem concerns the delivery by forceps of the fetus with threatened or early asphyxia, as diagnosed by alterations in the rhythm of the heartbeat, usually slowing. We now know that "traumatic cerebral asphyxia," often followed by generalized asphyxia, is not uncommon. The effect of applying forceps to a head already traumatized may be to increase the trauma and kill the child instead of saving it. I still follow the traditional practice of delivery with forceps if the head is low and the os full, in cases of fetal distress; but the point has now become a controversial one.

The prevention of injury in breech labor has already been referred to. As for the so-called "prophylactic forceps" operation, I am not impressed by the arguments of those who advocate it (J. R. Goodall, and DeLee), possibly because of a traditionally conservative training, but largely because of what I have learned at first hand about intracranial injury. The deep episiotomy is a disadvantage to a childbearing woman, in that it prevents her from losing the disadvantageous state of nulliparity as far as her pelvic floor and perineum are concerned. As regards induction of premature labor, so far as the child is concerned it should be restricted to cases of real necessity, and they are very few. F. Browne has proved that cerebral hemorrhage is sixteen times more frequent in premature than in mature babies; and there is, besides, a considerable neonatal morbidity and mortality.

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8 QUEEN ANNE STREET

DISCUSSION

DR. HUGO EHRENFEST, St. Louis, Mo.—That the fetal head in the course of labor can sustain more or less marked traumatic injuries has been known for a very long time. Some of those present may recall the amusing discussion of possible damaging effect of labor on the child's head, presented about 175 years ago, by Laurence Sterne in his delightful *Life and Opinions of Tristram Shandy*. There he describes how by the tremendous expulsive force of the laboring uterus the lax and pliable head is compressed and molded into "the shape of an oblong, conical piece of dough." Whimsically Tristram's father exclaims: "Good God! what havoc and destruction must this make in the infinitely fine and tender texture of the cerebellum." "No wonder the intellectual web is so rent and tattered as we see it."

Just about a hundred years ago, Cruveilhier presented in his pathologic-anatomic atlas some excellent illustrations of intracerebral hemorrhages observed in newborn infants. Accurate information in regard to the anatomic nature of such damage began to accumulate with the introduction, by Beneke in 1919, of a new method of opening the infant's skull at autopsy. In this manner was revealed the important fact that most often the intracranial hemorrhages are the result of an injury to the dura and especially of the tentorium. This brief historical survey must be concluded with the statement that we owe to the studies of Professor Holland the present clear insight into the mechanical factors which cause certain dura folds to tear.

In contrast to all other mammals, in whom the skull of the newborn is a solid capsule and intracranial injuries are unknown, the cranium of the human fetus consists of loosely connected flat bones. This permits the required changes in configuration of the head during the second stage of labor, and thus its adaptation to the varying spatial conditions at the various levels of the bony pelvic canal. Molding does not result in any reduction of the volume of the skull but solely in alterations of its shape, the shortening of diameters by compression in one direction being accompanied by a corresponding lengthening of diameters in a perpendicular direction. It is the function of the dura folds to prevent excessive lengthening in certain directions, and therefore excessive compression in another direction. Dr. Holland has taught us to understand these strains and stresses developing within the cranium.

The intimate relation of intracranial damage to difficult or unskillful forceps extraction or to quick expulsion of the head as the result of an overdose of pituitrin is generally recognized. This fact by itself cannot, however, be used as an argument against any effort to shorten or lighten the discomforts of the parturient woman by operative interference. The continued, forcible pounding of a fully compressed head in the pelvic outlet against a rigid pelvic floor certainly implies greater danger to the fetus than an episiotomy followed by the gentle lifting out of this head with a forceps.

Strains of a different sort arise during the passage of the aftercoming head in a breech labor. It is surprising that obstetricians, even many who write textbooks, still fail to appreciate that fetal death in breech labor is only rarely due to asphyxiation, as formerly thought, but as a rule to intracranial damage, most often as the result of undue haste applied for the purpose of avoiding the presumably dangerous asphyxiation. The timely and correct extraction of the head by means of Piper's forceps undeniably affords to the aftercoming head great protection against injury.

However, the best prophylactic measure against damage to the aftercoming head is an external version gently done about six weeks before term without the use of any anesthetic.

It seems to me a significant fact that statistical records, first supplied by German clinics, ascribing about one-fourth of all fetal loss during labor to fatal intracranial injuries, have been consistently confirmed by reports later coming from all parts of the world. There undeniably are marked differences in the rates of operative deliveries in Great Britain, France, Japan, Brazil, Holland, and the United States, but everywhere careful autopsies in large series made on all newborn infants, stillborn or dying within the first forty-eight hours, uniformly show a 25 per cent mortality due to intracranial damage. In our fetal mortality statistics the incidence of birth injuries as the certified cause of death is gradually increasing but still remains far below the figure of 25 per cent where it should actually be. Physicians have become better acquainted with this important cause of fetal loss and are becoming less afraid to enter this diagnosis on the death certificate.

It is true that for our country the rates both of birth injury deaths and operative deliveries are increasing, but this does not necessarily prove an immediate connection between these two facts. In my opinion these two rates have increased as the result

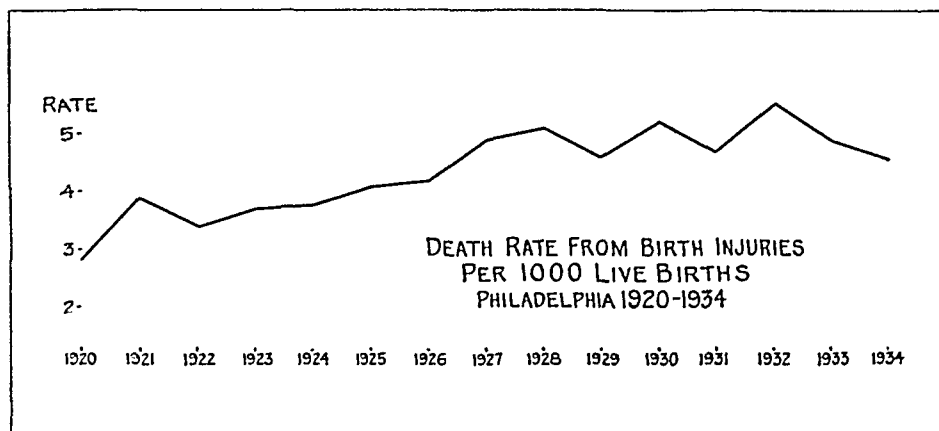


Chart 1.

of the remarkable increase in hospital deliveries, incidentally leading to more autopsies and more correct diagnoses of the cause of death. In the year 1935 a little over 13,000 babies were born in the city of St. Louis and over 10,000 of them, about 79 per cent, in hospitals. This seemed to me a strikingly high percentage, but I have just heard from Dr. Williams that also in Philadelphia the percentage of hospital deliveries amounts to 80 per cent of the total.

DR. PHILIP F. WILLIAMS, PHILADELPHIA, PA.—The first slide shows the frequency of birth injury in the stillbirths in the seven states and two cities which make up the stillbirth registration area of the United States. In 1933 the total stillbirths in that area were 17,000, of which about 22 per cent were caused by the type of birth injuries which Dr. Ehrenfest mentioned. I think we can consider that the dystocia group and probably a great many of the malpresentation group undoubtedly represent intracranial injury. We see therefore that a very large proportion of the deaths from birth injuries are occasioned by intracranial injuries.

The death rate among women who gave birth to stillborn babies is from four to eight times as great as in those giving birth to live babies.

From these graphs it will be seen that the death rate from birth injury has increased in the city of Philadelphia in the last decade and a half, slowly but surely. Whether this is due simply to the better recognition of birth injury deaths is hard

to say. Of course, Table I includes asphyxia and other causes of death, but a large proportion of these deaths must undoubtedly be due to birth injury.

Chart 2 shows the death of infants under one month from 1920-1934 in Philadelphia. The hospitalization of maternity cases has increased during this period from 18 per cent in 1920 to 80 per cent in 1934. Of course, we know that there are more obstetric operations performed in hospitals than upon patients treated at home. Whether that makes any difference we cannot say. The high peak was reached in 1932 when one out of every five children dying under one month died of birth injuries. We hope the recession at the present time will continue.

We know that in many of these intracranial lesion deaths the tear is of slight degree and the amount of hemorrhage is minimal. I would like to ask Dr. Holland to explain a little further the actual causation of death where at autopsy we find so little actual injury in that type of lesion.

We all know that the injury Dr. Holland described is not the only type of lesion that causes death. Any fetus that dies at birth necessitates an examination of the entire cerebrospinal system. A large proportion of birth injury deaths are occa-

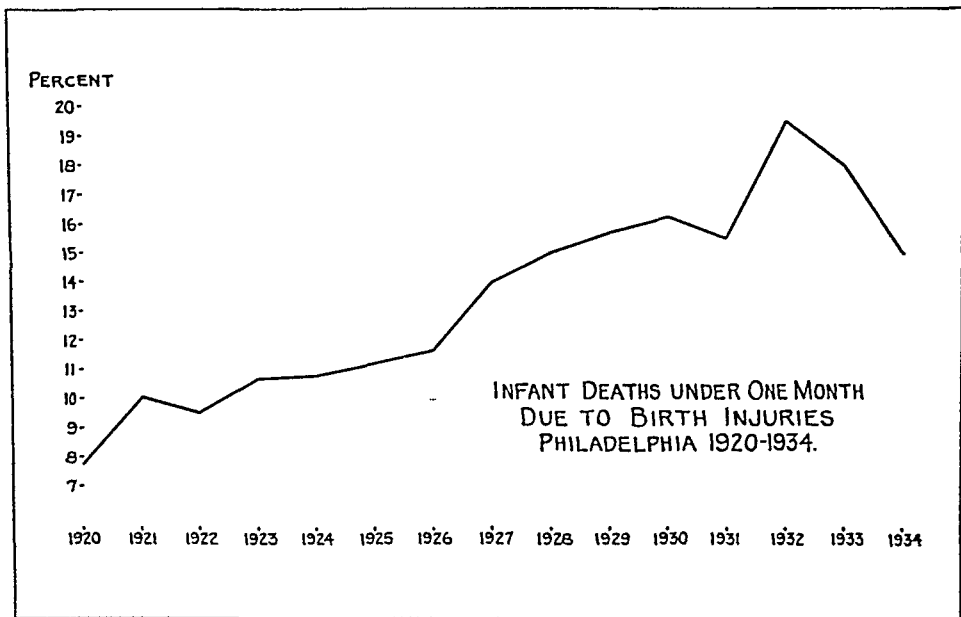


Chart 2.

sioned by the depression of the occipital bone with resulting pressure on the cerebellum. There have also been found large numbers of dislocations of the spinal column where intracranial injuries were also present. I would like to ask Dr. Holland to explain what part the change in the intracranial pressure plays in these cases.

TABLE I. NUMBER OF STILLBIRTHS DUE TO BIRTH INJURIES IN AREA FOR WHICH STILLBIRTHS ARE TABULATED BY CAUSE BY THE U. S. BUREAU OF THE CENSUS, 1933

CAUSE OF STILLBIRTH	NUMBER	PER CENT DISTRIBUTION
Total stillbirths	17,207	100
Due to birth injuries	5,097	30
Antepartum hemorrhage and hemorrhage of uterus	45	---
Placenta previa	443	---
Prolapse and compression of cord	1,568	---
Malpresentations	718	---
Difficult labor	1,495	---
Asphyxia of child (cause not stated)	828	---
All other and not specified or unknown	12,110	70

When we come to the discussion of prevention of birth injury deaths, we can sum up that the two most important points in prevention are wider application of the known principles of antenatal study of our patients and a more thorough consideration of the selection and technic of necessary operations.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—Dr. Holland's little antelope was not only born without a forebrain and with closed fontanelles, but was also born with face presentation. I preface my remarks thus because my experience has convinced me that in great measure the intracranial damage of the fetus occurs during the passage of the broadest diameters of the head through the inlet. That is where molding is at its maximum. That is when the tentorium and the falx are exposed to the most continuous and severe strains and stresses, and this is the location in which the severe lacerations occur.

It is perfectly true that continuous pressure during the second stage of labor while the head is in the birth canal may lead to asphyxia and to some degree of brain injury, yet experience with cesarean section in cases of dystocia convinces one of the fact that the major injuries take place in the pelvic brim. This of course takes no account of outlet compression, wherein great injury may result.

The figures of Sharp of New York, in which he obtained the bloody cerebral spinal fluid from lumbar punctures in 10 per cent of children following all types of delivery and including cesarean section cases consecutively, proves conclusively, to my mind, that it is not the ordinary type of forceps delivery which injures the child but the extreme molding and compression, which occur at the inlet.

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—Dr. Holland has opened up a very wide field for discussion of a problem which is agitating many people at the present time. He has referred specifically, however, as one of the main causes of fetal death, to dystocia, from malformations of the pelvis and ill-adaptation of the fetal head, and to an increased number of forceps deliveries. I think there is another factor which must be considered when we take up the subject of neonatal deaths, namely, the anesthetics and the analgesics so widely used today. Of course, the propaganda for painless labor has reached all classes and both wives and husbands come to the obstetrician with a demand that they desire a labor which shall cause as little pain as possible. Is it not to be considered that we have gone a bit too far in our promises to produce painless labor by the use of anesthetics and analgesics? Admitting, as we must, that it is necessary in some cases, analgesia in a large majority increases the length of labor and frequently interferes with the natural expulsive forces, necessitating instrumental interference in a great many instances. The use of nitrous oxide so commonly employed in the final stage, may delay delivery in many instances and produce a degree of asphyxia in babies which is not generally recognized. Dr. Eastman in his recent studies has brought out some of these facts. The same thing applies to the use of the barbiturates and the pharmacologists are now telling us that they may be transmitted to the fetus, passing through the placenta, and they have actually been found in the fetus and the amniotic fluid. Now, such delays in the natural processes of labor and such effects of anesthetics on the fetus must bear, it seems to me, a considerable share of the blame for these neonatal deaths.

The use of the prophylactic forceps does not seem to me to cause as much damage, especially in the terminal stage when the woman is unable to push that head over the perineum, as the use of the drugs that interfere with fetal respiration. I believe that we must not only regard instrumental deliveries as a factor in the production of these fetal deaths, but must also consider the various anesthetics and analgesics. A generation ago, before we knew much about the barbiturates, before we knew much about gas-oxygen anesthesia, we used chloroform by the drop method,

and I often feel that for the instruction of medical students and of the general practitioner in obstetric procedures, it might be well if, instead of stressing the employment of these other measures, we went back perhaps to the inhalation anesthetics. Their administration can be regulated and it seems to me that they cause less damage so far as the prevention of asphyxia neonatorum is concerned.

DR. PAUL TITUS, PITTSBURGH, PA.—Dr. Ehrenfest might have continued his quotation from Tristram Shandy somewhat further, thus emphasizing that this problem of whether “to forcep or not to forcep” is already several centuries old.

You will recall that when Dr. Slop was called because Mrs. Shandy had fallen into labor, he left home in such a hurry that he forgot to take with him his instruments. These were his tire-tête, his crochet, his squirt, and his new invented forceps, which were left hanging, in a green baize bag, on his bedpost. Consequently when the omission was discovered, Obadiah, the man-of-all-work, was dispatched post-haste on horseback to fetch them.

Obadiah, fearing to lose the instruments while galloping back, tied the strings of the bag into a double hard knot. When he arrived, Dr. Slop had so much difficulty in getting the knots untied that there was considerable doubt whether he would be able to get at his forceps before Mrs. Shandy should deliver herself spontaneously.

DR. JAMES R. GOODALL, MONTREAL, CANADA.—I regret to have to disagree with Dr. Schumann, when he states that injuries of the baby's head occur at the pelvic inlet. It is well known that birth injuries occur in a large number of cases where there is absolutely no disproportion, and they also occur most frequently in primiparas. Therefore, they cannot be due to any disproportion between mother and child, but are the results of dystocia of the soft parts.

Birth injuries occur in the first and second stages of labor, but in the first stage, only when the labor is dry. The majority of cases occur in the second stage, and are due to asphyxia, which is of two types, the acute and cumulative. The acute is the result of prolonged spasm of the uterus, while the cumulative is due to the child carrying over a percentage of anoxemia after each pain, when the uterine pains are unduly long and the intervals too short to permit complete aeration.

There is nothing more productive of brain hemorrhage than high grades of anoxemia. Much of the damage it has done to the baby's head has been attributed to the use of forceps. The use of forceps is unduly delayed in the majority of these cases, and the damage to the baby's head has already occurred before they are applied. The injury is, nevertheless, attributed to the pressure of the forceps, although it has been proved recently, by my own writings, and those of others, that the frequent use of prophylactic forceps has reduced the incidence of brain injuries over 50 per cent.

A very easy test to determine whether the baby is suffering from brain hemorrhage as a result of dystocia or the fetal heart distress is merely due to asphyxia is found in the use of chloroform. If one administers chloroform under these circumstances, one finds the fetal heart rate returns to normal very quickly, if there is only asphyxia, but if brain hemorrhage has occurred, the return of the fetal heart to normal does not take place. This test seldom fails to give one accurate information concerning the child's cerebral state.

DR. FRED L. ADAIR, CHICAGO, ILL.—Dr. Holland emphasized the relative immaturity of the term “fetus.” I would like to stress that point, carrying it back a little farther in gestation, stressing the idea that the premature fetus is much more susceptible to these injuries than the fetus at term. There are a certain number of patients with chronic disease in whom it may be necessary to terminate

the pregnancy and to perform an operation for sterilization. In these cases cesarean section may afford a much better prognosis for the infant, especially if premature.

I am in agreement with Dr. Goodall that while intracranial injuries may occur from injury at the inlet, the most frequent cause of intracranial injury is after the head has passed the inlet. It is not only the degree of compression of the head, but the duration of that compression which is an important factor.

Many of these intracranial injuries either occur or are aggravated by delivery through the outlet. I would like to stress again the importance of depression of the occipital bone in association with deliveries through the outlet, and also to mention the likelihood of the Ritgen maneuver with forcible pressure against the pubic arch being a possible cause of intracranial injury.

DR. HOLLAND (closing).—I do not think that the death rate from birth injuries is increasing. What is increasing is correct certification, and the very fact that in cities like Philadelphia 80 per cent of the babies are born in hospitals surely will favor correct certification.

Dr. Williams asks a very important question, namely how to account for death in cases where there is scarcely any cerebrospinal hemorrhage or any injury. It is due to what I call traumatic cerebral asphyxia. If the head is subjected to sufficient pressure and to sufficiently prolonged pressure, the intracranial tension will so rise that the cerebral sinuses and veins are obstructed with the result that the brain and medullary structures become asphyxiated. When the brain and medullary centers become asphyxiated, the respiratory center is stimulated. If the fetus makes respiratory efforts, the intrathoracic pressure becomes negative and there is a pouring of blood into the thorax. There will then arise venous obstruction of the heart and the accompanying rise in intravenous pressure will give rise to these petechiae which I showed you on the screen. Of the cases to which Dr. Williams referred nearly all show very intense development of petechiae. If the asphyxia continues, the center becomes paralyzed and the baby dies in utero. That, I think, is the explanation of the deaths in these cases of trauma which do not show gross injury, but what I call traumatic cerebral asphyxia.

I may also repeat what Dr. Goodall said. I think the pelvic reserve is immense, as the radiogram or a typical examination shows. Furthermore nearly all of the head has gone a long way past the brim before labor starts, and I do not think there is damage to the head as it is going through the brim unless there is pelvic disproportion.

I agree with Dr. Kosmak about analgesics, but we have got to give them, for if we do not nobody will come near us. I think barbiturates are very dangerous indeed, and believe they kill mothers and also babies.

Seguy, J.: *Etiological and Clinical Study of Sterility*, Rev. franç. de gynéc. d'obstét. 31: 280, 1936.

The problem of sterility has become too complex. To achieve success in its solution it is essential for the biologist, chemist, pathologist, and physiologist to work together with the gynecologist. Also the urologist must cooperate because it is illogical to dissociate male sterility from female sterility. Biochemists interested in research on hormones should prove especially helpful in the study of sterility.

J. P. GREENHILL.

INCONTINENCE OF URINE IN THE FEMALE*

SOME FUNCTIONAL OBSERVATIONS OF THE URETHRA ILLUSTRATED BY ROENTGENOGRAMS

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(From the Clinic of the Woman's Hospital)

THIS paper is an unprejudiced endeavor to evaluate the loss of urethral function that women suffer who are afflicted with incontinence of urine, and to develop a method whereby I might improve my disheartening results while trying to alleviate this disturbance. No congenital defects, no vesicovaginal fistulas, no absence or loss of the urethra, no case with a known impaired nerve supply, and no operative procedures are included. The paper is a study of the function of the urethra in cases where the nervous control of the urethral sphincter is considered to be functioning normally. The urethra with normal function, before labor or operation upon the anterior vaginal wall, which to have lost some of its control following labor or operation, seems to me has suffered injury to the muscle or supporting structures of the sphincter mechanism and has preserved its nervous control unimpaired. On this assumption the study was begun.

Incontinence of urine in the female, if present to such a degree that any form of exertion makes the patient wet her clothes, drives her to give up routine social duties. She seeks a hospital where she pins her hope on getting relief, is operated upon and leaves, in many instances, with little or no improvement over her previous state and is sometimes worse. From this time on she remains at home, believing that any further attempt to relieve her will be of no value. If she likes to go about and does not wish to be an invalid, she justifiably makes this fact known in the hospital and I admire her persistence. If she submits to further operation and fails in a second attempt, she will give up, and we do not get further opportunity to help her. Being continually wet she is burdened with a condition more distressing than rectal incontinence where, in many instances, the escape of feces is only intermittent.

Reports of results and failures are taken from three papers. H. A. Kelly and William M. Dumm,¹ reported on 20 cases of incontinence with success in 16, or 80 per cent, and complete failure in 4, or 25 per cent. B. P. Watson,² reporting on 105 cases followed after operation, had complete success in 65.7 per cent (2 out of 3), had 21.9 per cent where the control was better than before operation, and 12.4 per cent (1 out of 8) with no improvement. H. Dawson Furniss³ reports his results in 21 cases, 8 being minor in character, 9 having marked incontinence, and 4 having complete incontinence. In his follow-up 4 of these patients

*Read at a meeting of the New York Obstetrical Society, March 10, 1936.

were not heard from. Of the 17 cases, 6 were mild, all of which were successes; of 7 who had marked incontinence, 5 were successes, 1 was a partial success, and 1 was a failure; of the 4 with complete incontinence, 2 were successes, 1 was moderately benefited, and 1 was a failure. In the 17 cases, 13 were complete successes or 76.5 per cent, while there were 2 failures or 12.9 per cent.

Marion Douglass,⁴ in a recent study, states: "the anatomy of the vesical neck is insufficiently understood. The vesical neck is produced by thickening of the musculature and submucosa which forms the layer about the orifice which functions as a sphincter, i.e., the sphincter vesicae internus. In addition, but in the female essentially, continuous with the structure of the vesical neck there is an external sphincter which is essentially voluntary in function." Victor Bonney⁵ feels that while there is a sphincter it is only one factor in the sphincter mechanism and probably the least important, and there is probably still a good deal of ignorance on the subject.

The nervous mechanism cannot be overlooked. The bladder has three such mechanisms: (1) Intrinsic within the bladder musculature, the weakest of the nervous controls; (2) the lower spinal cord reflex, having perhaps the strongest control; (3) voluntary control, acting from the cerebrum through the abdominal muscles. In the urethra the external sphincter is smooth muscle with motor and inhibitory impulses passing between it and the hypogastric ganglion. Afferent motor impulses pass from the posterior urethra through the pudic nerve to the anterior primary division of the sacral nerves and back to the external sphincter. The internal sphincter is smooth muscle and is under the control of the hypogastric ganglion with motor and inhibitory impulses passing between them. Whether there is any voluntary control surrounding the urethra and whether there is more sphincter control than at present acknowledged is a question I have asked myself. Wherein does the supporting structure play a part?

Victor Bonney⁵ speaks of observing a layer of tissue with fibers running transversely below the urethra and probably some fibers surrounding the urethra, some of these fibers being muscle. He found the bladder attached to the back of the pubis by thin fibers. Edward Martin,⁶ in his atlas, *Der Hafterapparat*, Plate IV,⁵ illustrates the attachment of the bladder to the posterior symphysis. Fibers begin in the middle umbilical ligament, spread out over the anterior wall of the bladder longitudinally and come together, separate portions attaching themselves to the posterior of the symphysis forming the pubovesical ligament. B. P. Watson found that out of about every three patients having incontinence, two had cystocele as a complication. He states further that "in all patients presenting this symptom there is a marked sagging away of the bladder from its proper situation behind the pubis; very often it is a marked sagging of the whole of the anterior vaginal wall and bladder in the form of a cystocele. In many, however, the cystocele may not be pronounced, or may be absent. In some cases of complete procidentia where both vaginal walls are completely everted, control may be perfect; in such it will be found that the neck of the bladder remains braced up in its normal situation. The sagging of the neck of the bladder away from the back and under aspect of the symphysis is very easily demonstrated by introducing a catheter or sound into the bladder. On exerting a little pressure the lower end of the anterior vaginal wall can be made to bulge at the vaginal orifice and a small stream of urine will often escape alongside the instrument. I believe that it is this sagging of the neck of

the bladder with its surrounding sphincter away from its normal attachment, rather than damage to the sphincter itself, which is the cause of incontinence. The sphincter has lost its *point d'appui*, and so fails to act efficiently.' His operation consists in a very careful and thorough dissection and suturing to restore these supports. Victor Bonney does a similar procedure and believes that failure results because the attachment of the pubocervical ligament has become loosened beyond where it can be repaired from below.

Realizing that the best follow-up published shows a failure of one in eight, and knowing that my own were very much inferior, I felt that we should not send our failures away but should make a study of their condition. They really need our help and if we are able to relieve them then the easier ones should give no trouble. Consequently, at the Woman's Hospital, I began to study patients who presented themselves for the first time, patients who became incontinent following operation for cystocele who previously were continent and patients who had failed to get relief after one or more operations. Roentgenograms of the bladder are not new. Charles C. Norris a number of years ago showed the funnel shape of the bladder opening into the urethra.

METHOD OF OBTAINING ROENTGENOGRAMS

In the beginning a simple rubber sac was connected to a manometer in which the roentgen opaque fluid was a solution of sodium iodide. Pressures could be measured at the time pictures were made. The contour of the urethra could be outlined but little stretching of the sphincter muscles of the urethra could be obtained because of the extreme elasticity of the sac wall.

A new apparatus was designed (Fig. 1). A metal tube *C* 6 cm. long was taken and a rigid arm was attached at one end. Rotating about it was a guard *G*, which, when in contact with *C*, could be kept close to the external meatus of the urethra. The guard *G* was so placed that the tube *C* could extend 1 cm. into the urethra. The sac *S* was a two-layer membrane—the outer fishskin, the inner very thin rubber—was about 2.5 cm. in diameter when fully dilated and was firmly attached to *C* at the point where the guard *G* came in contact with it. The length of the sac *S* was about 5.5 cm. Connected to the other end of *C* was a rubber tube leading to the manometer *M*. The manometer, connecting tube and sac were filled with a 25 per cent solution of sodium iodide and the level of the surface of the solution in *M* above the level of the urethra measures the pressure in the sac. Strongin suggested that pictures of the bladder should be taken at the same time, consequently 200 c.c. of a 3 per cent solution of sodium iodide was put in the bladder before the sac was put into the urethra. To insure a uniform manometer pressure in that portion of the sac in the bladder, a section of a ureteral catheter *A*, with a metal collar *K* at one end and a cork *B* for the other was made and this ran from one end to the other as illustrated in Fig. 2.

The steps in making a picture are as follows:

1. Prepare the patient similarly as for a cystoscopic examination. Introduce a catheter to allow all urine to run out of the bladder, then introduce 200 c.c. of a 3 per cent solution of sodium iodide through the catheter into the bladder and remove the catheter. Now insert *A* into *D* through its open end *F*, then push *D* into *C* and this acts as an obturator to introduce the sac into the urethra sufficiently

far for the guard *G* to rest against the external orifice of the urethra. Attach a 20 c.c. Luer syringe containing 25 per cent sodium iodide solution to *L*, the end of *D*, and slowly empty the contents of the syringe into the sac while *D* is with-

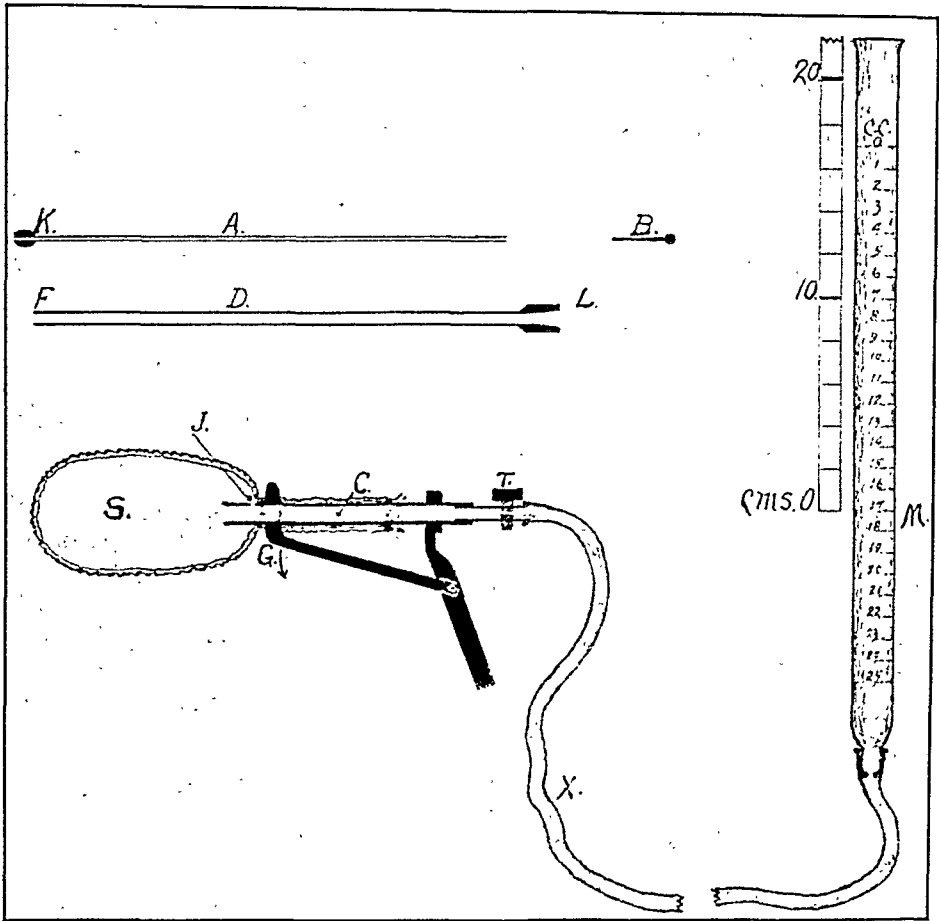


Fig. 1.

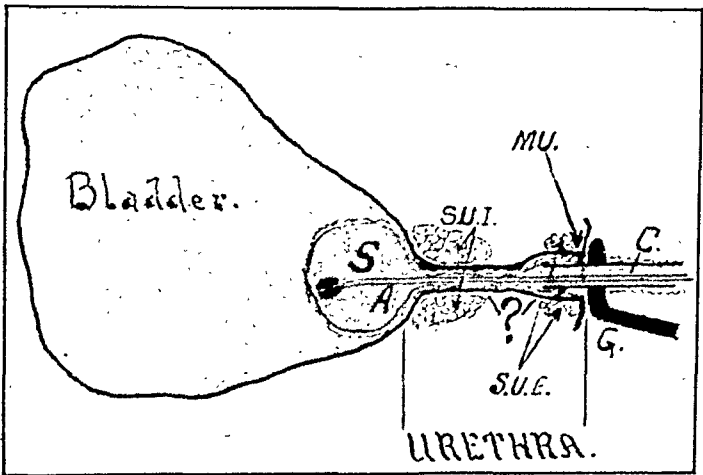


Fig. 2.

drawn, leaving *A* within *C*. Attach the manometer tube to *C*. Raise the manometer tube *M* to obtain the desired pressure in the sac. Each picture obtained reveals separately the contour of the bladder and the contour of the urethra, since the solution in the bladder has different opacity from the solution in the sac. The

relationship of the bladder to the urethra can be observed and at the same time the pressure in the sac is always at right angles to surface, consequently at right angles to the inner surface of the urethra. The pressure in the urethra is equal and opposite in direction to the force exerted at right angles to the urethral sphincter muscles as they contract to prevent the escape of urine from the bladder. When the pressure in the sac is varied, one can arrive at an estimation of the efficiency of the sphincter control. The involuntary sphincter control is mainly exerted by fibers about and near the internal and external thirds of the urethra. For arbitrary reasons in this paper the urethra has been divided into an inner, a middle, and an outer third; and the efficiency of the sphincter about each portion is estimated. Pictures were made at different pressures when a patient was relaxed (R throughout), i.e., when she made no effort to void and no effort to hold her urine. Pictures were also made with a constant pressure (1) when relaxed (R throughout), (2) when an effort to hold her urine was made (H throughout), and (3) when an effort to void was made (V throughout the paper). The following insignia appear in the illustrations: *SUI* sphincter internal urethra; *SUE* sphincter external urethra; *MU* external urethra; *VUO* vesicourethral orifice.

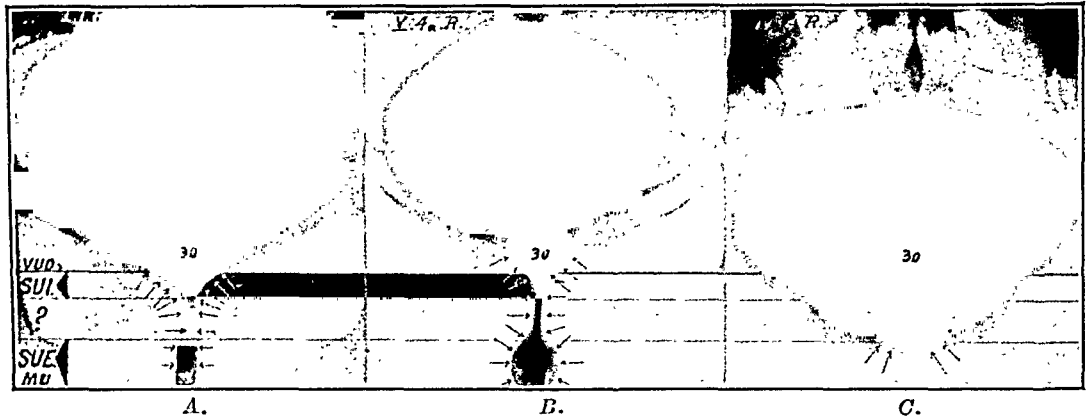


Fig. 3.

Three roentgenograms appear in Fig. 3: The first (A) is a roentgenogram of a normal urethra and bladder with 30 cm. of fluid pressure in the sac. The external pressure exerted by the urethral sphincter is in the direction of the arrows. It will be seen that the pressure which the sac exerts against the internal sphincter tends to stretch it outward from the urethral axis and the counter pressure exerted by the internal sphincter tends to force this part of the sac with fluid in it farther into the bladder which tends to make the remainder of the sac a cylindrical wall. However, the middle third of the urethra has some sphincteric force about it greater than 30 cm., since the urethra is here constricted. An entirely different picture appears in B. Here we see the external sphincter stretched out to a considerable diameter, the internal sphincter less stretched and nearly normal, but the middle third still has a sphincteric constricting force greater than 30 cm. of fluid pressure. In this particular instance the sphincter action about the middle third is greater than that about either the outer or the inner third. Here the inner also has a greater constricting force than the outer.

C presents a rather distressing picture, where, under 30 cm. of water pressure the sphincteric force about both the inner and middle thirds of the urethra have been completely overcome and only the external sphincter is exerting any constricting force. This patient has a definite incontinence. This leads one to believe that there is a third sphincter surrounding the middle third of the urethra, having a greater constricting force than the sphincter surrounding either the inner third

or the outer third. The sphincter about the internal third is normally stronger than the sphincter about the outer third. Further on in this paper the author will present evidence to show that the inner third is protected and will function better when the sphincter about the middle third is strong and functions well, and is well supported. One here asks himself the question: Is this sphincter about the middle third smooth muscle and a continuation of the inner sphincter fibers, and in addition supported by a sling of voluntary muscle fibers, holding it up under the pubic arch by attachments to each posterior aspect, or is it composed of both smooth and striated fibers, the striated fibers surrounding the urethra and having their ends attached to the posterior aspect of the symphysis? Either arrangement would satisfy good function and any operation to restore such anatomical function should restore continence where incontinence exists.

CASE REPORTS

CASE 1.—This patient, aged twenty-three years, complained only of sterility; had no dysuria, no nocturia, but had a retroverted uterus. The pictures taken of this patient's urethra and bladder shown in Fig. 4 are consequently of a *normal* urethra and bladder and were made when she was relaxed, i.e., making effort neither to hold her urine nor to void. The pressure in the sac was varied, and pictures were

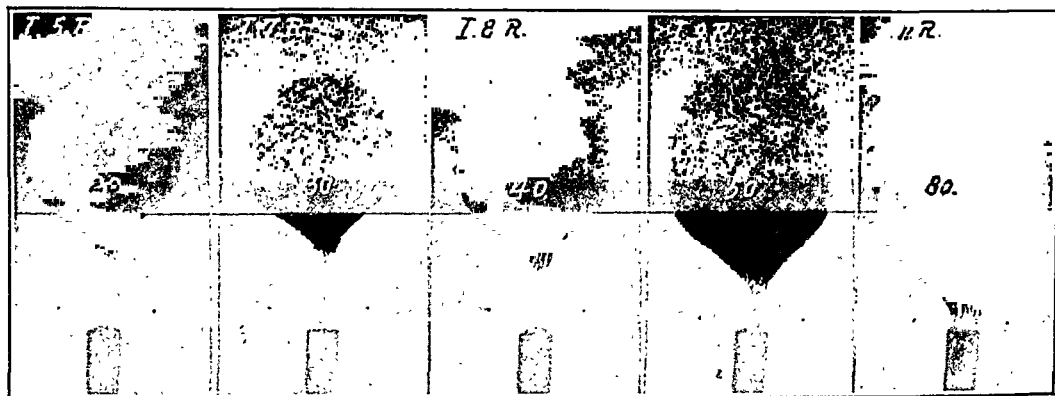


Fig. 4.

taken at 20 cm., 30 cm., 40 cm., 50 cm., and 80 cm. It will be noted that the first indication of the internal sphincter's dilating takes place between 30 cm. and 40 cm. fluid pressure. The middle third of the urethra does not begin to dilate until a pressure between 40 cm. and 50 cm. is reached, is not nearly stretched at 50 cm., and still has some sphincteric control at 80 cm. of pressure.

CASE 2.—This patient was in the hospital first in 1933, and complained of incontinence of urine for previous eight years. She had had 8 full-term pregnancies, the last in 1923. No repairs were done at delivery. Incontinence had become progressively worse. She wore a pad constantly and any walking or straining caused leakage. When lying down there was little loss of urine. Wassermann was four-plus; urine negative; operation, dilatation and curettage, amputation of cervix, operation for incontinence (Kelly stitch), operation for cystocele, rectocele, and lacerated pelvic floor. Still had incontinence when she appeared for her ninth pregnancy in 1934. Pelvic floor repaired at this delivery. Incontinence persisted. Entered the hospital in 1935 for another Kelly stitch, which was still a failure. Fig. 5 represents a series of pictures taken at 0, 10, 20, 30, and 50 cm. fluid pressures successively. The internal sphincter appears as much dilated at 20 cm. as the normal did at 40 cm. pressure, and much more dilated at 30 cm. than the normal was at 50 cm. Most of the sphincter about the middle third of the urethra has been set aside at 30 cm. pressure.

This patient was operated upon by a new method which has given her complete continence of her urine and pictures made fifty-two days after operation are shown in Figs. 11 and 12. Fig. 11 shows the comparison of the sphincter function before and after operation at 30 cm. pressure when the patient was relaxed. Fig. 12 is a composite picture: the dots represent the position of the bladder and urethra in a state of relaxation and the dashes illustrate the position of the bladder and urethra while the patient endeavors to void. One sees that the effort to void does not press down the urethra and that the sphincteric action about its middle third has been restored.

CASE 3.—This patient, aged forty-one years, had had three full-term pregnancies and was badly lacerated. A prolapse of the uterus appeared and she was operated

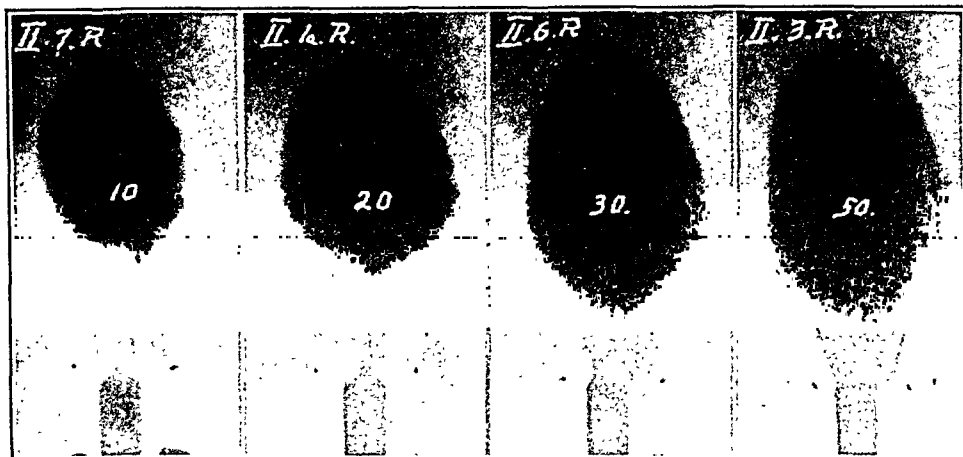


Fig. 5.

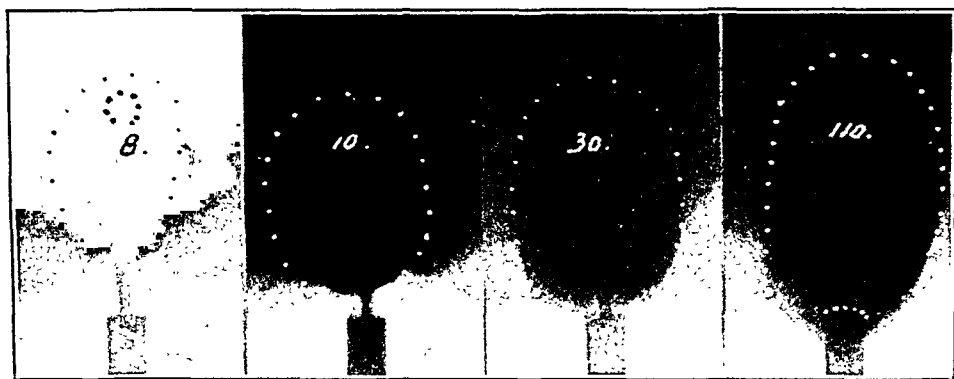


Fig. 6.

upon for the prolapse, but one year later it recurred as did also a cystocele. The incontinence was more marked. Roentgenograms were made and are shown in Fig. 6 at pressures of 8, 10, 30, and 110 cm. successively. It is noted that the middle third of the sphincter of the urethra is more set aside at 10 cm. pressure than the normal was at 80 cm., that at 30 cm. pressure the external sphincter begins to be pressed out and at 110 cm. pressure much of the external sphincter has been stretched.

CASE 4.—This patient, aged thirty-three, had had two full-term pregnancies, the first instrumental. Complained of something coming down, urgency and frequency, but no incontinence. Had metrorrhagia with frequent clots. A dilatation and curettage, amputation of the cervix and operation for cystocele were done. Operation with wide dissection was done and two sutures (Kelly stitch) were placed below

the urethra. Fig. 7 shows three composite pictures of lateral views. The upper shows how much more urethral sphincter is pressed aside at 25 cm. than at 10 cm. The middle shows the excursion of the urethra from a position of relaxation to one of voiding at 25 cm. pressure. The lower shows that at both relaxation and voiding at 25 cm. pressure the sac remains the same size.

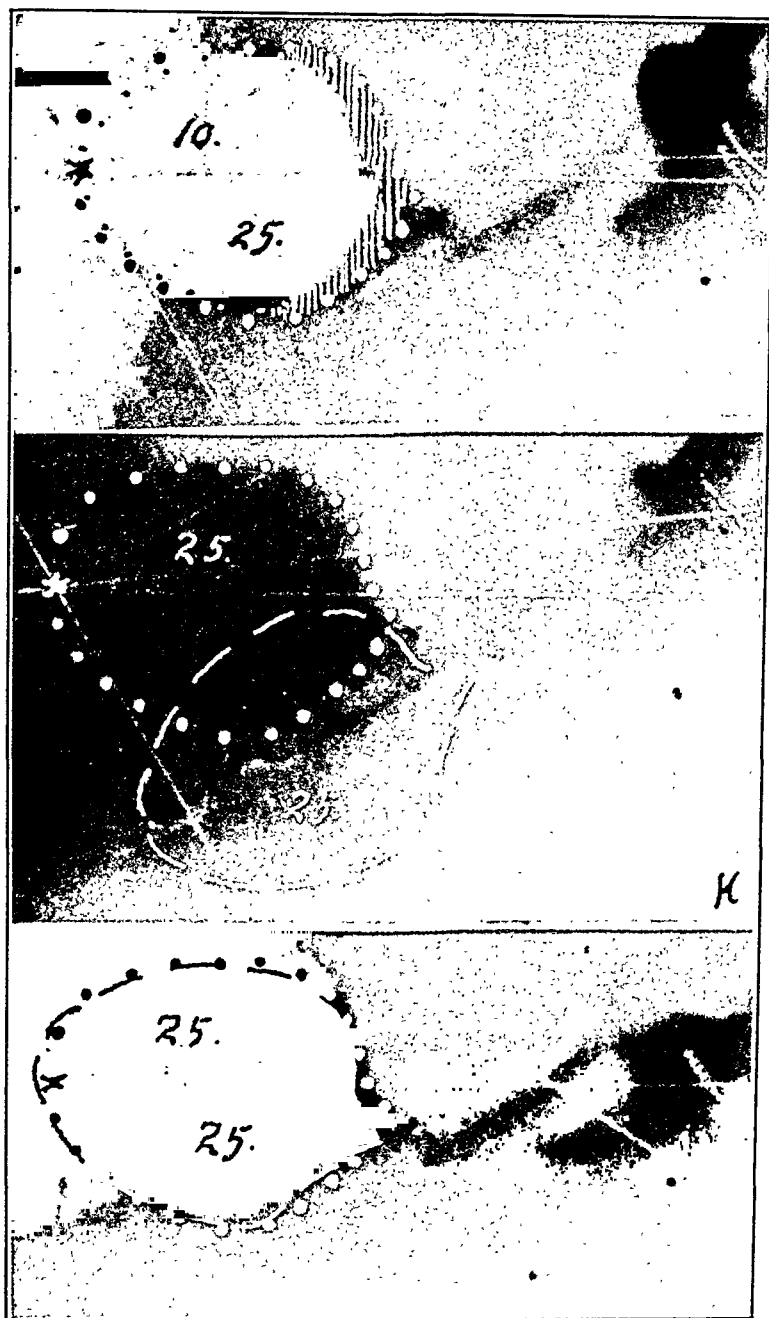


Fig. 7.

CASE 5.—This patient, aged forty, had had incontinence for two years. She had a large myoma which distorted the bladder and apparently pressed also on the urethra. The operation consisted of a supravaginal hysterectomy, separation of adhesions and a bilateral salpingo-oophorectomy. One month after operation she still had some incontinence but this is much improved. Fig. 8, the first picture, shows a marked stretching of the internal sphincter and considerable stretching of the sphincter about the middle third when she is relaxed. However, the second

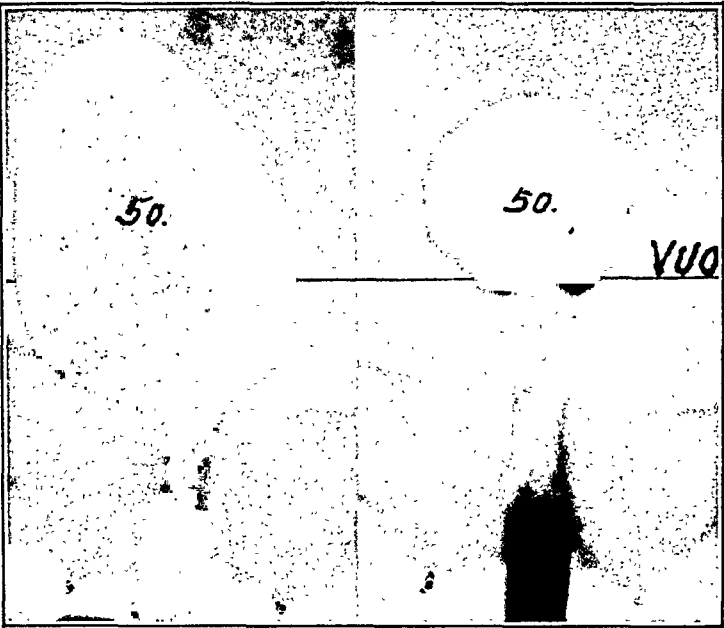


Fig. 8.

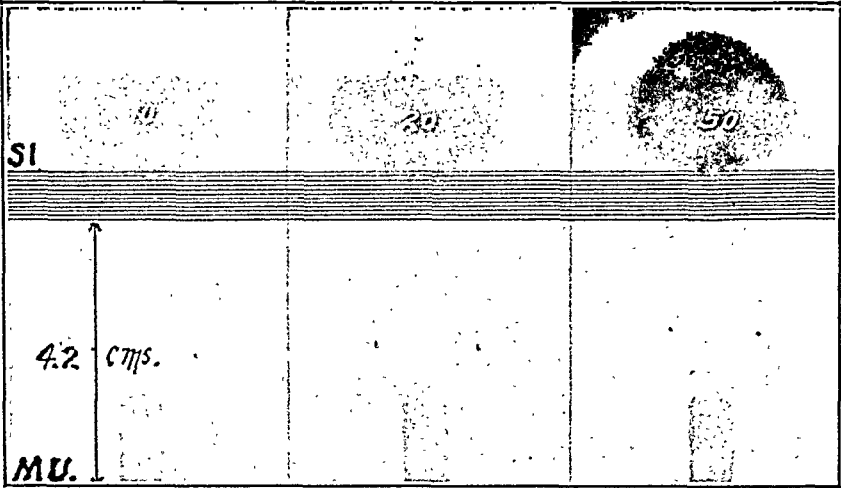


Fig. 9.

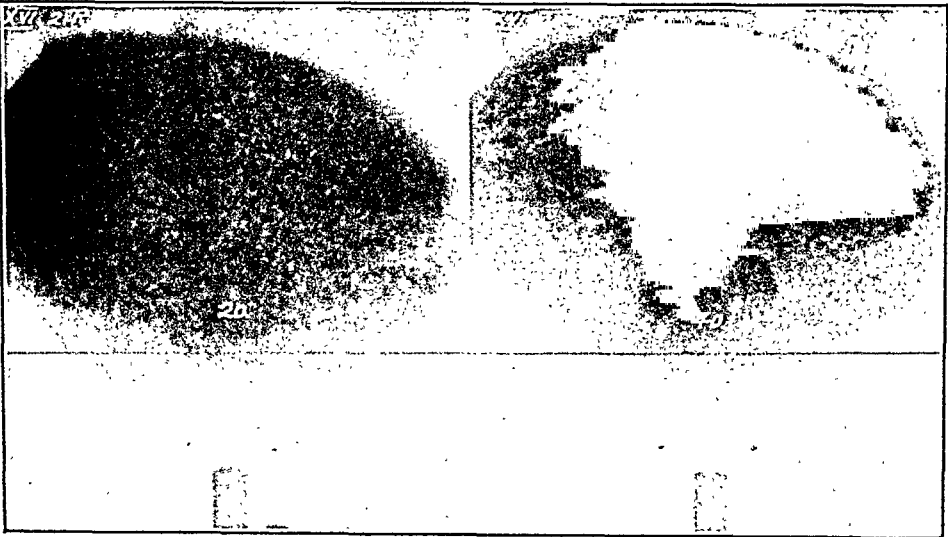


Fig. 10.

picture, taken while voiding, shows she can empty the sac and at the same time constrict both the internal sphincter and the sphincter about the middle third even at 50 cm. pressure.

CASE 6.—This patient, aged forty-three years, had no incontinence but only frequency and urgency. She had had one full-term pregnancy. Due to difficulty of catheterizing, a stricture of the urethra was found which began 4.2 cm. from the external meatus. Fig. 9 illustrates a urethra which does not stretch even about the inner third. The width of the stricture is shown by the parallel lines. The

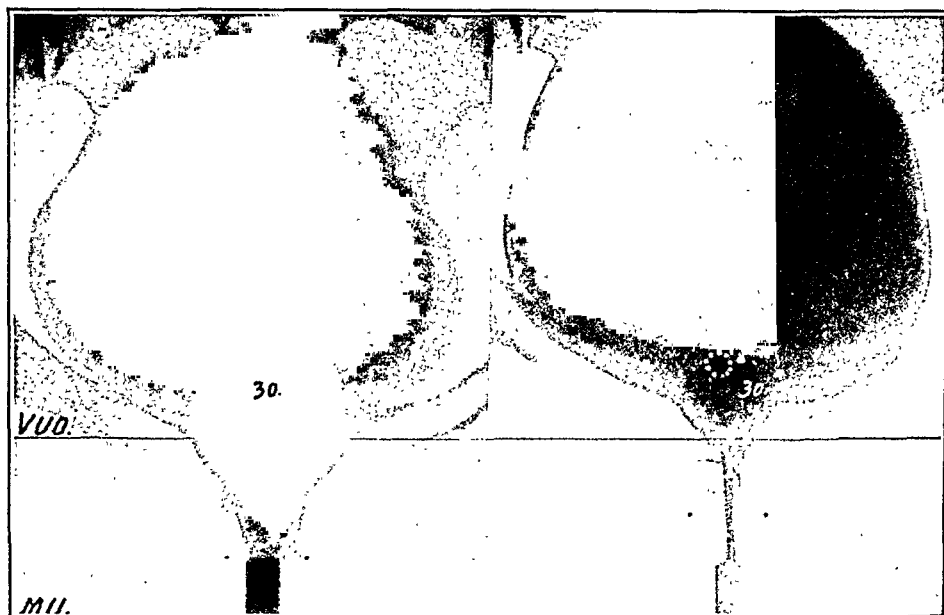


Fig. 11.



Fig. 12.

stricture here acts as a guard near the junction of the middle and inner thirds, preventing any undue strain from injuring the inner third sphincter and allowing it to function normally.

CASE 7.—This patient, aged thirty-eight, complained of incontinence while laughing, sneezing, and coughing. She has had 6 full-term pregnancies and she was torn at the birth of the first child. The operation done one year ago consisted of a dilatational curettage, an amputation of the cervix, and a reconstruction operation for incontinence, but the incontinence was worse after operation. Unfortunately the study on this case before operation was one of the earlier cases and was of no value.

She has had a complete hysterectomy and appendectomy. The bladder was separated from the anterior vaginal wall well down below the trigone and plicating sutures were placed about the inner third of the urethra and in the trigone. Fig. 10 illustrates the urethra at pressures 20 and 40 cm. successively in the sac. Much similarity appears in this picture to the one where the stricture existed; the sutures apparently constricting the inner third of the urethra. Three months after operation the patient was continent and symptom-free. This stricture seems to support and fortify the sphincter about the inner third, enabling it to function much more effectively.

CONCLUSIONS

1. The average length of the urethra is between 4 cm. and 4.5 cm., and there is a sphincter muscle around it throughout its whole length.

2. While there is an involuntary sphincter muscle about each of the inner and outer thirds of the urethra, there is an additional sphincter about the middle third which is probably under voluntary control. This control is greater than that of either involuntary muscle.

3. The interposition of the uterus between the bladder and the vaginal wall will not improve an incontinence, but plication of the urethra near the trigone will in some instances produce a mild stricture and help much to restore continence.

4. There is a pressure (about 30 cm. of fluid) which, if when exerted it stretches the sphincter about its middle third, justifies one's suspecting some degree of incontinence.

5. The causes of incontinence are (1) trauma of the inner and middle third sphincters of the urethra causing them to become partially fixed by fine bands to the posterior lateral margins of the adjacent pubic rami, and (2) damage in the midline to those voluntary fibers which pass under the middle third of the urethra and are attached to each ramus of the pubis, posteriorly constituting a "sling" support.

6. It is possible to relieve or cure incontinence by (1) breaking down the fine bands between the urethra and each posterior lateral portion of the ramus and plicating the urethra in its midline vaginally, to prevent any further connection with the ramus laterally and (2) bringing together in the midline beneath the inner and middle thirds of the urethra, the uninjured portions of the "sling" fibers which are themselves attached to the posterior of the ramus, in a lateral direction from the urethra. (Description of operation to appear in another article.)

The author extends his acknowledgment and thanks to Dr. George Gray Ward, Chief Surgeon of the Woman's Hospital, for the privilege of undertaking this study; to Dr. Edward A. Bullard for his generosity in assigning satisfactory cases to me; to Dr. A. J. Murphy for cystoscopic assistance; to Dr. H. C. McIntosh for her x-ray experience and suggestions and to Miss Helen Cronin for her skill in taking the roentgenograms.

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OVARIAN RUPTURE CAUSING INTRAPERITONEAL HEMORRHAGE*

WITH REPORT OF TEN CASES

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THE exact incidence of intraperitoneal hemorrhage resulting from rupture of the ovary, in the absence of pregnancy, is not known. Prior to the surveys of von Beust¹ and of Novak,² medical literature contained less than 50 single case reports. In 1926, Brakeley and Farr³ reported 15 cases. By 1931, the total of published cases had reached 94 (Morton⁴). The larger number of single cases and series reported during the last five years (Boggon and Wrigley,⁵ Sackett,⁶ Masson and Phillips,⁷ and Hoyt and Meigs⁸) indicates a growing appreciation of this clinical entity. More than 300 cases have been reported to date.

The earlier reports do not distinguish with sufficient clarity between follicle and corpus luteum rupture to warrant an estimate of the respective frequency of each as a cause of intraperitoneal hemorrhage. However, study of the more recent surveys indicates that corpus luteum perforation is by far the more common lesion. The preponderance of reported corpus luteum perforations may be explained, in part, by the fact that the resultant hemorrhages are greater and more productive of symptoms than those accompanying follicle perforations.

ETIOLOGY

Rupture of the graafian follicle is a normal occurrence in the ordinary cycle of ovarian activity. It is accompanied by little bleeding because the tenuously stretched point of perforation (stigma) is relatively avascular. However, moderate hemorrhage may occur when abnormal conditions which cause hyperemia of the thecal vessels adjacent to the stigma are present. Rupture of the corpus luteum, on the other hand, is an unnatural phenomenon and is generally accompanied by frank bleeding. The premenstrual hyperemia and capillary hemorrhage give rise to a corpus luteum hematoma (Teacher⁹) which, if sufficiently intense, may rupture spontaneously through the stigma, lacerate the adjacent thecal vessels and cause intraperitoneal hemorrhage.

In the presence of inflammatory ovarian congestion, or during the period of normal corpus luteum vascularization, sudden trauma may be the exciting factor (Shaw¹⁰). However, a history of trauma is difficult to evaluate. Corpus luteum perforation has occurred following

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an abdominal blow (Christopher¹¹), during quiet sleep (Johnston¹²), and during coitus (Klein,¹³ Payne,¹⁴ Johnson,¹⁵ and Stuckert¹⁶). Ovarian rupture has occurred during the performance of ordinary activities, such as walking, dancing, and washing clothes (Novak²). The possibility of ovarian rupture and intraperitoneal hemorrhage following bimanual (pelvic) examination is known to gynecologists (Crousse,¹⁷ Greenhill,¹⁸ Pratt,¹⁹ and Novak²). Schumann,²⁰ having demonstrated focal endarteritis in several instances of ovarian rupture, is of the opinion that normal ovaries do not give rise to massive hemorrhage. Ovarian hyperemia resulting from chronic oophoritis may give rise to abnormal ovulation (dysovulation) and hemorrhagic follicular rupture (Hirshfeld²¹). The opinion of Forssner,²² that most ovarian perforations are unrecognized examples of ovarian pregnancy, is not generally supported.



Fig. 1.—Photomicrograph of wall of perforated corpus luteum cyst showing dense, fibrinous layer between cavity and lutein layer (Case 8).

PATHOLOGY

The amount of free blood found in the peritoneal cavity after ovarian rupture may vary from one-half ounce to several liters. If the origin of the hemorrhage is a perforated graafian follicle only serosanguineous fluid may be present, but frank bleeding usually occurs when a richly vascularized corpus luteum ruptures. The reaction of the peritoneum itself is that of active hyperemia, the intensity of which varies with the degree of hemorrhage.

The ruptured portion of the ovary is usually adherent to the posterior surface of the uterus and exhibits a hemorrhagic exerescence of varying size. Following expression of the clot, the hematoma cavity presents a smooth, glistening interior of yellow hue. The latter is not pathognomonic of exposed lutein (corpus luteum) cells, and must not be employed as the criterion of identification. The yellow color may be de-

rived from lutein cells, lipid deposits, blood pigment within phagocytes or luteinized theca interna cells (Teacher,⁹ and Robinson²³).

Histologically, the origin of the ovarian hematoma may be a graafian follicle, an atretic follicle cyst, a maturing corpus luteum or a corpus luteum cyst. The graafian follicle is distinguished by the membrana granulosa and the clumped, crowded cells of the theca interna. The atretic follicle cyst is recognized by the flattened or entirely atrophic



Fig. 2.—Photomicrograph of wall of perforated corpus luteum cyst showing marked alteration of the lutein cells (Case 7).

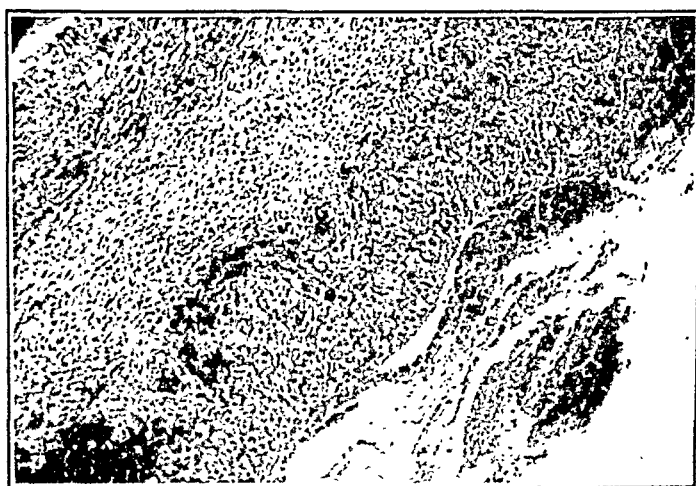


Fig. 3.—Photomicrograph of wall of perforated, mature corpus luteum showing part of the central hematoma, well-preserved lutein cells, interstitial hemorrhage, and V-shaped bands of theca interna (paralutein) cells (Case 1).

granulosa cells, and the well-preserved (often luteinized) theca interna cells. The maturing corpus luteum and the corpus luteum cyst are easily differentiated. The latter usually contains a firm, central hematoma which is separated by a dense, fibrinous layer (Fig. 1) from the unrecognizably altered lutein cells (Fig. 2). The mature corpus luteum is characterized by a loose, central hematoma and a layer of large, well-

preserved lutein cells. The appearance of the latter is modified by the newly formed capillaries, mild hemorrhage and the penetrating bands of paralutein cells (Fig. 3).

Inasmuch as dual lesions may occur, complete pathologic study should be made of all tissue removed during any laparotomy for ovarian rupture. Hematosalpinx (Greenhill¹⁸), ectopic pregnancy (Novak²), and acute appendicitis (Hoyt and Meigs⁸) have been reported in association with ovarian hemorrhage. One of our patients (Case 2) had an unruptured tubal pregnancy in addition to perforated corpus luteum. As shown by two patients of the present series (Cases 6 and 8), the excised appendix may show a definite inflammatory reaction of its outer layers (serosa and subserosa), in response to the irritation caused by free blood in the peritoneal cavity.

SIGNS AND SYMPTOMS

Ovarian rupture with intraperitoneal hemorrhage may occur at any time during the childbearing period, but it is more often seen in young women. The average age of several groups of patients reported recently^{3, 7, 8} was no more than twenty-five years. Eight of the 10 patients herein reported were less than thirty years.

A characteristic relationship exists between the time of ovarian rupture and the menstrual cycle. Follicular rupture occurs at approximately mid-interval, and corpus luteum rupture during the last half of the cycle. As suggested by Pratt,¹⁹ rupture of a graafian follicle with mild intraperitoneal hemorrhage may be the cause of mid-interval pain in certain women (Mittelschmerz). The time of corpus luteum rupture seems to be fairly constant, as illustrated by the fact that all 10 of the corpus luteum perforations presented below occurred during the premenstruum. This inherently functional relationship to the ovarian cycle is an important diagnostic feature and serves to distinguish between follicular and corpus luteum rupture.

The clinical manifestations of ovarian perforation may be either sthenic or asthenic, varying with the size of the perforation and the degree of hemorrhage. The patient with asthenic symptoms may appear quite comfortable, despite the considerable amount of free blood within the peritoneal cavity. The sthenic type, on the other hand, may be introduced by violent pain or shock. Between both extremes, all gradations of the acute abdomen may be present. The most prominent symptom is abdominal pain of sudden onset and variable intensity. It is more often localized in the right lower abdomen because of the more frequent involvement of the right ovary,^{5, 7, 8} although right-sided pain may occur with left ovarian rupture (Block,²⁴ and cf. Cases 3 and 4). Nausea and vomiting are frequent accompaniments of the abdominal pain. Shoulder pain (referred) may appear if the free blood sufficiently irritates the subdiaphragmatic peritoneum. Shock may modify the entire clinical picture in fulminating cases.

Moderate elevation of the temperature and polymorphonuclear leucocytosis frequently occur, varying in degree with the amount of hemorrhage. The erythrocyte sedimentation rate may be abnormally rapid because of the intraperitoneal hemorrhage. Unfortunately, the febrile reaction, the leucocytosis, and the sedimentation test are not sufficiently characteristic to be of diagnostic significance.

Tenderness on palpation of the iliac fossae and rigidity of the recti muscles may be present, more especially of the right side. Bimanual examination may delineate the ovarian hematoma as a soft, tender adnexal tumor. Such a mass is differentiated from a tubal hematocele of ectopic pregnancy with great difficulty. The amount of free blood is rarely sufficient to cause bulging of the posterior culdesac, though it may occur (Case 8).

DIAGNOSIS

The view that preoperative diagnosis of ovarian hemorrhage is not possible, is no longer tenable. Many instances of correct preoperative diagnosis have been recorded despite a generally "low index of suspicion" (Stokes) for ovarian rupture. Evidence of the value of a "high index of suspicion" may be found in the creditable record of the staff of the Massachusetts General Hospital where 17 of 58 ovarian perforations were correctly diagnosed prior to operation (Hoyt and Meigs⁸). Inasmuch as there is no pathognomonic sign or symptom, the diagnosis of corpus luteum or follicle rupture must be based on a careful analysis of the history. Evaluation of the symptomatology in the light of its relationship either to the time of ovulation or to the premenstruum is of diagnostic value. Ovarian rupture with intraperitoneal hemorrhage should be suspected in any woman presenting an acute lower abdomen, during the latter half of her menstrual cycle. The clinical picture being that of any acute abdomen, mild or fulminating, requires differentiation from all major abdominal lesions. However, it most closely mimics acute appendicitis and ruptured tubal pregnancy.

The erroneous diagnosis of acute appendicitis is frequently proposed, more especially in follicular rupture. The sudden onset of abdominal pain, nausea, vomiting, fever, leucocytosis, and tenderness in the right iliac fossa characterizes both conditions. The erythrocyte sedimentation rate may be a diagnostic aid, inasmuch as it is usually normal in appendicitis (Lesser and Goldberger²⁵) and increased by intraperitoneal hemorrhage. The presence of a palpable adnexal tumor favors the diagnosis of ovarian rupture. It may be virtually impossible to distinguish between acute appendicitis and ovarian rupture preoperatively. The attempt to accomplish this, however, should not be abandoned prematurely, because mild ovarian hemorrhage may not require surgical intervention. If reasonable doubt exists following an

exhaustive differential analysis, the diagnosis of appendicitis should be favored and a midline laparotomy performed.

The sthenic variety of ovarian rupture is usually diagnosed as ruptured ectopic (tubal) pregnancy. The presence of an adnexal tumor or culdesac bulging is not of differential value since it may exist in both conditions. The history is important, inasmuch as a preceding menstrual irregularity commonly occurs in ectopic pregnancy. In fulminating cases time should not be spent in establishing the exact diagnosis, because laparotomy is indicated in any case. However, if the clinical picture is mild and if a delay of from thirty-six to forty-eight hours is permitted by the patient's condition, the differential diagnosis may be aided by the Friedman pregnancy test. Since the test is relatively unreliable (32 per cent error) in ectopic pregnancy, only a *positive* reaction would be of diagnostic significance (Goldberger, Salmon and Frank²⁶).

PROGNOSIS

The prognosis of ovarian rupture (nonpregnant) is good, varying proportionately with the degree of hemorrhage. Many mild cases are of minor gravity and pass entirely unrecognized. Isolated instances of death from massive ovarian hemorrhage have been reported (Novak²). The collective review of 77 cases by Johnson¹⁵ in 1930, included 6 fatalities (7.8 per cent). No deaths occurred in the series more recently reported.⁴⁻⁸

TREATMENT

The advisability of operation depends upon the individual case. If appendicitis or ectopic pregnancy can be definitely excluded from the diagnosis, nonoperative treatment may be applicable in many instances of ovarian hemorrhage (Pratt¹⁰). In order to obviate the possibility of erroneous diagnosis, careful observation is the *sine qua non* of nonoperative therapy. Thus, if there is any doubt concerning the existence of a more serious lesion (appendicitis or ectopic pregnancy), laparotomy is indicated.

The patients exhibiting signs of marked hemorrhage require immediate operation. If shock is present, supportive measures (including blood transfusion, intravenous infusion of glucose solution, and external heat) are necessary adjuvants. The incision should be lower midline or paramedian. Whenever possible, the bleeding ovary should be conserved. The simplest procedure is to strip the hematoma cavity of its lining and approximate its walls with a fine catgut suture. Wedge-shaped resection of the ovary or oophorectomy may be required, if the bleeding is uncontrollable with sutures. The treatment required by any concomitant pelvic pathology should be performed, if the patient's condition warrants.

REPORT OF CASES*

The histories of ten patients are briefly recorded below. A summary of the more pertinent data appears in Table I.

CASE 1.—(Mount Sinai Hospital, No. 91489.) The first patient, B. M., aged twenty-five years, who had had menses of the type, $12 \times 30 \times 4$, reported that her last period had begun March 20, 1935. On April 19, 1935, she was seized with pain in lower abdomen and was nauseated. Her temperature was found to be 99.3° F., and her leucocyte count, 11,800. Examination showed a walnut-sized, cystic mass to the right of the uterus. At laparotomy free blood was found in the peritoneal cavity and a ruptured right ovary was adherent to the posterior uterine wall. An ovarian hematoma was resected and bleeding controlled by mattress suture. The pathologic report was hemorrhagic corpus luteum in the stage of vascularization (Fig. 3).

CASE 2.—(Mount Sinai Hospital, No. 61265.) R. B., aged thirty years, had had menses of the type $14 \times 28 \times 5$, but her last period on Jan. 5, 1931, had been scanty. On Jan. 12, 1931, she developed pain in the right lower abdomen with nausea and vomiting, but the temperature was normal and the leucocyte count only 10,200. Examination disclosed a tender, right adnexal tumor, the size of a hen's egg. Laparotomy disclosed an unruptured ectopic pregnancy in the right tubal isthmus, old blood in the posterior culdesac, and a firm clot protruding from the interior of the right ovary. Right salpingo-oophorectomy was performed. A pathologic report of hemorrhagic, mature corpus luteum and tubal pregnancy was made.

CASE 3.—(Mount Sinai Hospital, No. 61032.) Y. A., aged twenty-five years, with former menses of the type $15 \times 30 \times 4$, had had her last menstrual period on Dec. 6, 1930. On Dec. 18, 1930, pain began in the right lower abdomen, the temperature remained normal but the leucocyte count rose to 14,050. Examination revealed only tenderness in the right iliac fossa. At laparotomy the peritoneal cavity was found "filled with blood" and the left ovary bleeding actively, the latter being controlled by a running suture.

CASE 4.—(Mount Sinai Hospital, No. 49343.) M. R., aged twenty-one years, with menses of the type, $11 \times 28 \times 4$, had had her last period on Sept. 1, 1928. On September 22, pain developed in the right lower abdomen with nausea and vomiting, the temperature being 99.2° F., and the leucocyte count 24,000. Examination showed only McBurney point tenderness. Laparotomy disclosed serosanguineous fluid in the peritoneal cavity and a perforated left ovary. Left salpingo-oophorectomy was performed, the pathologic report being hemorrhagic, mature corpus luteum.

CASE 5.—(Mount Sinai Hospital, No. 50032.) H. R., aged twenty-two years, reported menses of the type $12 \times 30 \times 5$ and a last period on Oct. 29, 1928. On November 24, pain began in the right lower abdomen accompanied by nausea and vomiting. The temperature was 100° F., and the leucocyte count 8,000. Examination showed a right adnexal mass, hen's egg in size. Laparotomy disclosed a serosanguineous fluid in the posterior culdesac and a bleeding perforation of the right ovary. The ovarian perforation was closed by a single mattress suture.

CASE 6.—(Mount Sinai Hospital, No. 94663.) E. B. G., aged sixteen years, had had menses of the type $11 \times 30 \times 3$ and had menstruated last on Aug. 17, 1935. On September 8, pain began in the right lower abdomen, the temperature rose to 99.4° F., and the leucocyte count to 15,900. Examination showed only McBurney point tenderness. At laparotomy fresh blood was found in the posterior culdesac with a ruptured hematoma of the right ovary and a small, right parovarian cyst. Ap-

*Eight were collected from the surgical and gynecologic records of the Mount Sinai Hospital of the past ten years, and 2 from the gynecologic records of the Hospital of the University of Pennsylvania of the past five years.

pendectomy, excision of the parovarian cyst and ovarian resection were performed. The pathologic report was serosal and subserosal inflammatory process of the appendix (mucosa and muscle layer not involved), and mature corpus luteum.

CASE 7.—(Mount Sinai Hospital, No. 50403.) I. Y., aged twenty-two years, reported menses of the type, $14 \times 35-40 \times 5$ with her last period on Dec. 9, 1928. On January 13, pain began in the right lower abdomen with nausea and the temperature was found to be 99.3° F., the leucocyte count 24,000. Examination revealed a lime-sized, right adnexal mass. At laparotomy several blood clots were found in the posterior culdesac and an oozing rupture of the right ovary. A wedge-shaped ovarian resection was performed. The pathologic report was simply corpus luteum cyst (Fig. 2).

CASE 8.—(Mount Sinai Hospital, No. 40479.) K. S., aged thirty-four years, with menses of the type $13 \times 28 \times 3$, had had her last period on May 1, 1926. On May 18, 1926, abdominal pain set in with nausea and vomiting. A temperature of 96.5° F., and a leucocyte count of 9,400 were noted. Shock, restlessness, air hunger, a board-like lower abdomen and bulging of the posterior culdesac were present. At laparotomy the peritoneal cavity was found "filled with blood," the left ovary bleeding from a large perforation. Left salpingo-oophorectomy and appendectomy were performed. The pathologic report was serosal and subserosal inflammatory reaction of the appendix and tube and corpus luteum cyst (Fig. 1).

CASE 9.—(Hospital of the University of Pennsylvania, Gyn. No. 22835.) P. W., aged twenty-seven years, with menses of the type $12 \times 28 \times 5$, had had her last menstrual period on June 13, 1933. On July 12, pain began in the left lower abdomen, with vomiting, but the temperature was normal and the leucocyte count only 11,600. Examination disclosed a small, tender left adnexal mass. At laparotomy, there was found free blood in the posterior culdesac and a large, bleeding rent in the left ovary. The hematoma was stripped out and the rent was closed with sutures. The pathologic report was hemorrhagic corpus luteum cyst.

CASE 10.—(Hospital of the University of Pennsylvania, Gyn. No. 23202.) H. B., aged forty-three years, with menses of the type $12 \times 28 \times 3$, had had her last period on October 14, 1933. On October 30, she was seized with pain in the lower abdomen but the temperature remained normal and the leucocyte count was only 8,000. A pelvic mass of grapefruit size, probably the uterus, was noted on examination at laparotomy. A free blood was found in the peritoneal cavity with several

TABLE I. ANALYSIS OF TEN PATIENTS WITH INTRAPERITONEAL HEMORRHAGE FROM CORPUS LUTEUM RUPTURE

PATIENT	AGE	RELATIONSHIP TO MENSES		ACTION WHEN RUPTURE OCCURRED	ADMISSION LEUCOCYTE COUNT	DIAGNOSIS PREOPERATIVE
		LENGTH OF CYCLE (DAYS)	DAY OF RUPTURE			
1	25	30	29	Coitus	11,800	Tubal abortion
2*	30	28	Menstruating	Walking	10,200	Tubal abortion
3	25	30	13	Dancing	14,050	Acute appendix
4	21	28	21	Typing	24,000	Acute appendix
5	22	30	25	Walking	8,000	Acute appendix
6	16	30	22	Playing tennis	15,900	Acute appendix
7	22	35-40	34	Eating	24,000	Acute appendix
8	34	28	18	Sleeping	9,400	Ruptured ectopic
9	27	28	27	Playing bridge	11,600	Tubal abortion
10†	43	28	16	Riding in auto	8,000	Myoma uteri

*Unruptured tubal (isthmic) pregnancy also present.

†Myoma uteri also present.

myomata uteri, and a ruptured hematoma of the left ovary. Supravaginal hysterectomy and left salpingo-oophorectomy were performed. The pathologic report was fibromyomas of the uterus and hemorrhage corpus luteum cyst.

SUMMARY

1. The clinical and pathologic features of ovarian rupture (nongravid) are presented. Corpus luteum perforation is shown to be a more frequent cause of intraperitoneal hemorrhage than is follicular rupture.

2. The characteristic relationship between the time of ovarian rupture and the menstrual cycle is described. Follicular perforations occur at mid-interval and those of the corpus luteum during the latter half of the menstrual cycle.

3. The differential diagnosis between ovarian rupture, acute appendicitis, and ectopic pregnancy is discussed.

4. The treatment of ovarian rupture is usually laparotomy with conservation of the bleeding ovary. Nonsurgical treatment may be permitted if the diagnosis is certain.

5. Ten cases of corpus luteum rupture with intraperitoneal hemorrhage are reported.

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Villard: A New Case of Pregnancy Following a Salpingostomy, Bull. Soc. d'obst. et de gynec. 25: 305, 1936.

The author reports the fifth case in his personal series of salpingostomies where a pregnancy followed this operation. Two of the women had abortions but another one who first had a miscarriage subsequently had three children at full term.

J. P. GREENHILL

EVALUATION OF SALPINGOSTOMY AND TUBAL IMPLANTATION FOR THE TREATMENT OF STERILITY*

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DURING the last few years great interest has been shown in operations on the fallopian tubes to overcome sterility. Obstructions in the tube are usually located at the fimbriated end or at the cornual end, but the closure may be present only in the midportion or in combination with other areas of obstruction. The types of operation generally performed to correct complete tubal closure are as follows:

When the occlusion is at the fimbriated end, simple release of adhesions may suffice to restore the patency of the tube (salpingolysis). More frequently, however, the distal portion of the tube must be removed or incised, and in one of many ways a permanent opening is made (salpingostomy). When an obstruction exists only in the midportion it is best to remove the site of obstruction together with the distal portion of the tube and perform a salpingostomy on the proximal portion. This is simpler than removing that portion of the tube containing the obstruction and suturing the incised ends in apposition. If the obstruction is in the uterine end of the tube, the operation generally performed consists of the removal of the cornual part of the tube together with a portion of the uterine corner and implantation of the distal, normal tube into the uterine cavity (tubal implantation). A second way to treat tubal obstruction situated at the cornual end is to remove the entire tube and implant half of the corresponding ovary still attached to its pedicle on the cornua (Estes operation). A third operative procedure to overcome obstruction at the cornua consists of the removal of the tube and implantation of the entire ovary inside the uterine cavity (Tuffier operation). In this paper, however, we are concerned chiefly with salpingostomy and tubal implantation.

SALPINGOSTOMY

Nearly every author who refers to the historical aspect of this operation makes the statement that the first salpingostomy was performed by A. Martin in 1885. However, Isbruch maintains that A. Martin and Schroeder performed this operation independently at the same time.

A. Mackenrodt reported two successful cases in 1894. From 1885 to 1895 Martin performed 62 salpingostomies. He followed 47 of these patients but only two became pregnant after the operation. In 1911, Gellhorn reported a successful case

*Read at a meeting of the Chicago Gynecological Society, May 8, 1936.

and mentioned that the literature of Germany, France and America contained 13 other cases of equally good results. In the discussion of this paper Bovée mentioned that he had done several salpingostomies, but that only one pregnancy occurred, which was an ectopic. In 1919, Bullard reported 3 pregnancies after 44 operations and in 1920, Seitz observed two abortions after 22 operations. In 1922, Child reported that he had observed 8 full-term babies after 7 plastic operations on the tubes and Ritter reported 65 salpingostomies with 4 subsequent pregnancies. Only one of the latter gestations went to term, 2 ended as abortions, and one was an ectopic pregnancy. Unterberger reported 5 full-term pregnancies after 57 salpingostomies, and Isbruch delivered 3 babies after 14 operations. Fuchs followed up 34 out of 42 women who had salpingostomies and found that only two pregnancies supervened. One was an intrauterine and the other an extrauterine gestation. Solomons performed 25 resections of the fimbriated end of the tube which were succeeded by 6 pregnancies. He also performed 15 resections of the isthmus, following which he observed one uterine pregnancy and two tubal gestations. In a later article (1935) Solomons reported 28 pregnancies after 366 tubal operations, the largest number performed by a single individual. The 28 pregnancies occurred after the following types of operation: 18 resections at the fimbriated end, 4 resections at the isthmus and 6 resections at the interstitial part. In addition to the 28 uterine gestations there were two ectopic pregnancies, both after isthmial resections. The total incidence of pregnancy, therefore, in the 366 cases, was 8.2 per cent. In the discussion of this paper Meaker reported 10 pregnancies after 19 salpingostomies. One of these gestations was an ectopic.

Koenig reported one pregnancy following 20 salpingostomies and Paucot had one intrauterine and one ectopic pregnancy. Similarly, Stockaert encountered one tubal pregnancy. Geller performed 21 salpingostomies, with negative results; Fels failed to observe any pregnancies after 34 such operations. Topuse claimed successful results in 15 per cent of his cases of salpingostomy (number not stated), and Matwejewa observed 5 full-term gestations after 45 salpingostomies. Hasellhorst failed to observe a single pregnancy after 55 of these operations, but Coghlan reported 3 pregnancies after 17 salpingostomies.

Kerwin and Gellhorn performed 50 salpingostomies. Of the 28 women followed, 7 conceived (25 per cent). One of these pregnancies was an ectopic and one terminated in an abortion. In the discussion of this paper Polak mentioned that he had performed 51 salpingostomies, with ultimate success in 7 patients bearing 10 babies.

Schmitz performed 15 salpingostomies, 2 of which were followed by pregnancy. This author collected a series of 429 cases in which 43 full-term pregnancies (10 per cent) occurred.

Dworzak and Hajek reported 78 salpingostomies, and 52 of these patients were followed. Only one pregnancy took place, which was an ectopic. The patient died on the operating table. Schultze observed 10 pregnancies in a series of 150 plastic operations performed by himself and others. In his series of 600 cases of sterility the tubes were closed in 44 per cent. Pregnancy, however, occurred in 3 per cent of these cases and in only 6 per cent when surgery was performed on the tubes.

Von Graff recently (1936) collected a series of 568 salpingostomies and tubal plastic operations from the literature after which he found 60 pregnancies (10.5 per cent). Among these 60 pregnancies, 16 went to term, 33 ended in abortion, 5 were ectopic and in 6 cases the outcome was unknown. Hence, there were only 16 known full-term babies after 568 operations, an incidence of 2.8 per cent or one baby for every 35.5 operations. Von Graff's incidence of ectopic pregnancies is far too low, as may be gleaned from my discussion of the complications which occasionally follow salpingostomy (see below). Sixteen ectopic gestations following this opera-

tion, excluding Von Graff's own case, are listed. The names of authors are not mentioned in Von Graff's article, hence it is difficult to ascertain the individual sources of his statistics. Since he appends an extensive and accurate bibliography to his paper it is unfortunate that many ectopic pregnancies were overlooked in his review.

COMPLICATIONS AFTER SALPINGOSTOMY

The complications which have arisen following salpingostomy are as follows:

1. The mortality most likely has not been greater than for simple laparotomies, but a few opponents of plastic operations on the tubes maintain there is no justification for exposing any woman to the risk of a laparotomy simply to overcome sterility.

2. The postoperative morbidity is difficult to judge, but a few authors have noted a high frequency of febrile complications. Thus Fuchs reports that in spite of the great care exercised in the selection of his cases he observed that febrile adnexal inflammation occurred after salpingostomy in 16 per cent of them. Dworzak and Hajek state that peritonitis following salpingostomy occurs in many cases because there is no way to ascertain whether or not the tubal contents are sterile. A. Martin had two deaths from peritonitis. Odebrecht, Veit and Prochownik reported reactivation of infection with the formation of pyosalpinx in the tubes upon which plastic operations had been performed. These patients required another laparotomy for removal of the inflamed adnexa. Dworzak and Hajek believe that such infections occur much more frequently after salpingostomies than the reports in the literature indicate. In many instances, however, I feel certain the cases were not suitable for this type of operation. For example, histologic examination revealed that 7 of Ritter's 65 cases had tuberculous salpingitis and therefore, plastic operations should not have been performed in these patients. Only one of them became pregnant, resulting in an abortion.

3. Abortion has occurred frequently after salpingostomy. A number of factors may be responsible for this, but perhaps two important ones are the following: (a) The functioning portion of the tube which is left after operation is shorter than the normal tube, and it may be that the fertilized ovum reaches the uterine cavity before it has completely arrived at the proper stage for implantation in the uterine endometrium. (b) The condition which produced the closure of the tubes may be responsible also for the abortion.

4. Ectopic pregnancies have occurred with relatively great frequency. It is difficult to determine exactly how many salpingostomies have been performed throughout the world because by no means have all of them been reported. Furthermore, there are many brief reports in the literature of one or more successful cases observed by individual gynecologists, but the negative results rarely have been published, except from large clinics. Seventeen ectopic pregnancies have been reported in the literature by the following 16 authors, but, as the answers to the questionnaire indicate, there have been others: Bovée, Duffek, Dworzak and Hajek, Fraenkel, Fuchs, Von Graff, Glitsch, Kerwin, Meaker, Paucot, Prochownik, Ritter, Solomons (2), Stockaert, Tweedy and Wesenberg.

The cause of ectopic pregnancies following plastic operations on the tubes is not known. Mechanical obstruction in the region of the operation most likely is not a frequent cause. Complete closure, of course, prevents passage of the spermatozoa; but if there is an opening sufficiently large to permit fertilization the ovum can nearly always pass through to enter the uterus. Interference with normal tubal peristalsis as a result of the original disease or because of adhesions may be a cause. Likewise changes in the tubal mucosa brought about by the disease which was originally responsible for the tubal closure may be the cause of some of these ectopic pregnancies. However, an important factor in producing ectopic gestations is the predisposition to recurrence of ectopic pregnancies in some women. As is well

known, a definite proportion of women have a second tubal pregnancy in the presumably normal tube which is left behind. A fair number of the reported salpingostomies were performed on the remaining tube at the time an ectopic pregnancy was removed. Many of these plastic operations have enabled women to give birth normally but, on the other hand, a few of them have been followed by repeated tubal pregnancies. In some of these women the second tubal pregnancy probably would have occurred even if the plastic operation had not been done.

5. Other late disturbances may occur after salpingostomy. Dworzak and Hajek found that 75 per cent of the 51 patients on whom they had performed salpingostomies subsequently complained of pain, especially at the time of the menses. Eleven of these women developed masses in the adnexal region, one of which was found to be a pelvic abscess, and another proved to be a large tuboovarian cyst.

TUBAL IMPLANTATION

The first tubal implantation was performed by T. Watkins in 1896 (not 1897 as generally stated in the literature), on a patient who had previously had one tube removed and who had an adenomyoma in the isthmus of the remaining tube. Permeability of the tube was restored. A few months later the patient had a miscarriage. This case was reported by both Watkins and E. Ries. No mention was again made in the literature of a tubal implantation until 1921.

In that year Shaw reported a successful tubal implantation performed by Cullen. (It was my good fortune to see this patient in the Johns Hopkins Hospital Dispensary, and also to assist Doctors Cullen and Shaw at the operation.) The patient had a placenta previa at seven and one-half months. However, a year later Cullen reported on the same patient because she had given birth to a full-term child. This was the first case in which a living child was born after transplantation of a tube. The first tubal implantation in Europe was performed by A. Mayer in 1917 but he did not report the case until 1924. Other reports of this operation appeared in the literature in rapid succession by Phillips, Volkmann, Novak, Strassmann, Unterberger, Kiparsky, Mandelstamm, Cotte and Bertrand, Douay, Markoff, Pfeilsticker, Michaelis, Heuck, Szekely, Melinkow, Black, Fels, Kattermann, L. Fraenkel, Redenz, Heimann, Tavernier and Gonnet, Dauve, Bécélère, Von Graff, R. E. Watkins, Geyer, and Zimmermann. The pregnancy which Unterberger reported in 1925 was the first one reported in Europe following tubal implantation. The second successful outcome in Europe was the one reported by Mandelstamm.

In 1932, Reiprich collected 40 tubal implantations from the literature following which there were 6 pregnancies. However, in 1930 Markoff had found reports of 54 such operations with 9 pregnancies, of which 6 went to term and one was an ectopic. He himself performed 4 operations and observed one pregnancy. Bonnet, in 1933, reported that in the literature up to this time he had found only ten pregnancies which had gone to term, one premature labor at seven and one-half months (Shaw) and one ectopic pregnancy (Heuck). In 1934, Fels reported 4 tubal implantations performed in his clinic. Only one pregnancy resulted and this was intrauterine. However, labor terminated in a rupture of the uterus at the site of the tubal implantation after a spontaneous delivery. Fels attributed this accident to the fact that the patient became pregnant too soon after the operation. In one case (Unterberger) the patient became pregnant one month after operation.

A large series of tubal implantations performed by one individual was first reported by B. Solomons in 1927. Up to this time he had done 24 of these

operations. He was rewarded with 3 pregnancies, 2 of which went to term and one ended in abortion. In 1935, Solomons reported 6 pregnancies following tubal implantations. (The total number of these operations is not stated.) C. C. Norris obtained excellent results in his series of 8 plastic operations on the tubes. Three full-term pregnancies followed tubal implantation and another full-term baby was delivered after a salpingostomy. Geyer had one full-term pregnancy after 5 tubal implantations.

Heuck performed 7 tubal implantations which were followed by one full-term pregnancy and one tubal pregnancy. Brunner observed an ectopic gestation following tubal implantation, and Dawson reported the following interesting case of a woman who had had 4 ectopic pregnancies. After an ovum was removed from the left tube, a salpingostomy was performed on both tubes. Three years later the patient had an ectopic pregnancy in the right tube and after two more years she had a third ectopic gestation, this time in the left tube. Both salpingostomy openings were dilated. Nine years after this, another operation was performed for a fourth ectopic pregnancy, again in the left tube.

Von Graff recently reported 2 tubal implantations, the first of which was followed by the delivery of a full-term baby, but the second patient had a tubal pregnancy. In Von Graff's review (1936) he collected 70 tubal implantations, of which 26 were followed by pregnancies. In 23 instances the pregnancy went to term, one ended prematurely as a stillbirth, one terminated as an abortion, and one was an ectopic. This yields a total of 23 full-term babies after 70 tubal implantations, an incidence of 32.9 per cent. In view of the results of the authors quoted above, it is difficult to believe that this figure represents the true incidence of full-term pregnancies after tubal implantation. In the first place, many gynecologists have performed salpingostomies and tubal implantations, but they have not reported their cases because they have had no success with these operations. Thus, in the discussion of Solomons' paper before the Sixth British Congress of Obstetrics and Gynaecology, Sir Ewen Maclean said: "I have many times performed salpingostomy in cases of salpingitis with sealing but I cannot quote to this Conference any instance in which there has been a succeeding pregnancy." In the second place, it is certain that more than one ectopic pregnancy has been reported after tubal implantation. I have found reports of three ectopic pregnancies after tubal implantation (Heuck, Brunner, Dawson) besides the one reported by Von Graff himself.

COMPLICATIONS AFTER TUBAL IMPLANTATION

The same complications which followed salpingostomies have occurred after tubal implantation, namely, slight mortality, postoperative febrile complications, abortion, ectopic pregnancy, and late disturbances. To these should be added rupture of the uterus at the site of the tubal implantation (Fels' case).

RESULTS OF A QUESTIONNAIRE

In order to determine the sentiment of American obstetricians and gynecologists concerning salpingostomies and tubal implantations, a questionnaire was sent to the members of the American Gynecological Society and the American Association of Obstetricians, Gynecologists and Abdominal Surgeons. One hundred and seven replies were received.

The questions and a summary of the answers are as follows: (Table I.)

1. Number of salpingostomies performed.

Of the 107 individuals who answered, 53 (50 per cent) had never performed any salpingostomies. Of the remaining 54 who replied, 14 said they had done "a few" of these operations, 5 had done "many" and 40 reported from one to 173 salpingostomies.

2. Number of tubal implantations performed.

Eighty-eight of the 107 individuals (82.2 per cent) answered that they had never performed a single tubal implantation. Of the remaining 19, five had done "a few," one had done "many," four had done one operation, three had done 2 tubal implantations and one each had performed 3, 5, 10, 15, and 18 of these operations, respectively.

3. Were Rubin tests or lipiodol injections made after operation to prove patency?

Most of the answers indicated that Rubin tests and salpingograms had not been employed, but many of the operations had been performed a number of years before these diagnostic tests were introduced. In many instances the reconstructed tubes were found to be closed by the Rubin test or salpingography, and in other cases the tubes were patent but no pregnancies followed. When more than one salpingostomy was performed the highest incidence of tubal patency following operation was 75 per cent in "several" cases. In one series of 9 cases all the tubes were closed after operation.

4. Did any pregnancies follow operation?

- a. Went to or near term.
- b. Ended in abortion.
- c. Ectopic pregnancy.

Altogether 54 pregnancies were reported in the questionnaires. Of this number 10, or 18.5 per cent, ended in abortion; 8, or 14.8 per cent, were ectopic pregnancies, and 36, or 66.7 per cent, resulted in live babies. Among these 36 babies four previously reported by Norris are included. The number of salpingostomies specifically reported in the questionnaires was 521. In addition to this, 14 individuals stated that they had done "a few" and six stated that they had done "many" of these operations. If we arbitrarily consider 5 operations as "a few" and 20 as "many" we have 190 more salpingostomies to add to the 521 where the numbers were specifically stated. Hence, there was a total of about 711 salpingostomies. In addition to this, the specific number of tubal implantations reported in the questionnaires was 62. Five individuals stated they had done "a few" and one said he had done "many." Arbitrarily using 5 and 20, respectively, for the "few" and "many" we have a total of about 107 tubal implantations. Hence, the number of all plastic operations reported was 711 plus 107, or 818. Since 54 pregnancies of all types followed these operations, the incidence of both normal and abnormal pregnancy was 6.6 per cent, or one pregnancy for every 15 plastic operations. However, since there were only 36 live babies in the entire series, the incidence of live babies was 4.4 per cent, or one live baby for every 22.5 operations.

Some of the individuals obtained excellent results, as for example, Curtis and Gardner, who reported "about seven" babies after 12 salpingostomies and C. C. Norris who delivered 4 live babies after 10 tubal implantations and a few salpingostomies. Cullen operated upon one patient who had three children and a fourth pregnancy in short succession after a plastic operation and another patient who

had two children promptly after operation. However, others had very little success. Thus Litzenberg reports one live baby after about 25 operations, Cooke (and Lee) three pregnancies after 173 operations, Dickinson no pregnancy following 30 operations, and Bland not a single pregnancy after "100 or more" of these operations. Living babies were reported by Cooke, Cullen, Curtis and Gardner, Dieckmann, Douglas, Gellhorn (through Emmert), Greenhill, Holden, Litzenberg, Matthews, Newell, Norris, Rongy, Royston, Schmitz and Wynne. The ectopic pregnancies were reported by Dannreuther, Gellhorn, Greenhill (see case report), Matthews, McGlenn, Royston (2), and Sampson. Information of three additional ectopic pregnancies has been received from Šovak and Meaker.

5. If the pregnancy went to viability, how was the baby delivered?

Of the 36 babies, 24 were presumably delivered spontaneously, 11 by low forceps and one by cesarean section.

6. Did any complications follow the operation?

Two deaths from peritonitis and one pelvic infection were reported.

7. Do you believe salpingostomies and tubal implantations are useful operations? If not, why not?

Among the 107 questionnaires, 60 (56 per cent) opinions were definitely opposed to these operations, 19 (18 per cent) were distinctly in favor of them, 16 (15 per cent) said the operations were worth while occasionally, and 12 (11 per cent) expressed no opinion. The group of 60 men who opposed the operations consisted both of individuals who had performed these operations and those who had not. On the other hand, some of the 19 who were definitely in favor of the operations had never done one, in spite of the belief they expressed. Many of the men who either expressed no opinion or said the operations occasionally had a field of usefulness had never performed any of the operations themselves. Hence, in spite of the fact that these men were all specialists in obstetrics and/or gynecology, they were not enthusiastic enough to try these operations even once. The expressed and implied sentiment, therefore, of the majority of those who answered the questionnaires is that plastic operations on the tubes to overcome sterility are not worth while.

TABLE I

TABLE I	
Number of replies	107
Never performed salpingostomies	53 (50%)
Never performed tubal implantations	88 (82.2%)
* * * * *	
Number of salpingostomies performed	711
Number of tubal implantations performed	107
<hr/>	
Total operations	818
Total pregnancies	54 (6.6%)
(One pregnancy for every 15 operations)	
Total live babies	36 (4.4%)
(One baby for every 22.5 operations)	
Babies	36 (66.7%)
Abortions	10 (18.5%)
Ectopic pregnancies	8 (14.8%)
* * * * *	
Number of individuals against plastic operations	60 (56%)
Number of individuals for plastic operations	19 (18%)
Number who believe operations are sometimes worth while	16 (15%)
Number who did not express any opinion	12 (11%)

In contrast to the results elicited in the questionnaire is the information obtained from Meaker and Sovak who were not on the membership lists for the questionnaires but to whom I wrote personally because of their interest in the subject. Meaker has performed 22 salpingostomies but no tubal implantations, and he observed 11 subsequent pregnancies, of which two were ectopics. One woman had two babies. Sovak and Holden reported improved plastic operations on the tubes, and the results of Sovak's cases are as follows: After five operations (3 salpingostomies and 2 tubal implantations) on private patients, three pregnancies (60 per cent) followed, but one of these was an ectopic. The other two resulted in live babies. Among 30 clinic patients operated upon (22 salpingostomies and 8 tubal implantations) pregnancy occurred in 3 (30 per cent) of the first 10.

OVARIAN IMPLANTATION

Some gynecologists who are opposed to tubal implantation remove the entire tube with the uterine corner and implant a portion of an ovary on the exposed portion of the uterus. A few gynecologists transplant the ovary into the uterine cavity.

Von Graff collected 66 cases in which a graft of ovarian tissue was placed on a uterine horn or on a tubal stump. He reported 14 pregnancies (21.2 per cent) following these operations. However, since only 5 of these pregnancies went to term, only 7.6 per cent of the operations, or 1 in 13.2 operations, resulted in a full-term baby. Among the remaining 9 gestations, there were 6 abortions and one ectopic pregnancy. The outcome in 2 cases was unknown. In Von Graff's collected series of 41 cases in which an ovary was transplanted into the uterine cavity, only 3 pregnancies (7.5 per cent) resulted, of which one went to term (2.4 per cent) and the other two ended in abortion. Reiprich collected 200 ovarian transplants of all types and reported only 5 pregnancies (2.5 per cent) following these operations. Estes followed up 27 out of 88 patients on whom he had performed his ovarian transplantation operation and found that pregnancy had occurred in 4 of them (15 per cent). In a later article, Estes reported that in a series of 50 patients whose case records were complete, only 4 became pregnant (8 per cent). Two of these women had abortions and two had full-term babies.

Sovak states (personal communication) that four pregnancies resulted after the six Estes operations he had performed. Because of economic conditions three of these women had induced abortions but the fourth patient had a spontaneous abortion.

Some of the complications which I have described as having followed plastic operations on the tubes have also occurred after ovarian transplantation. Thus R. E. Watkins performed an ovarian transplantation and subsequently had to do another operation to remove the transplanted ovary which had grown to be a cystic mass 2 cm. in diameter, and which proved to be a chocolate cyst. Wier reported a death following an ovarian transplantation. This woman became pregnant following an ovarian graft but her uterus ruptured during labor. Autopsy revealed that the rupture had occurred at the site of the ovarian transplantation.

In a personal communication Mathieu described a case in which he removed a fallopian tube, made an opening in the cornu, and sutured an ovary into the uterus at this point. The patient became pregnant. Fearing that a rupture of the uterus might take place, Mathieu performed a cesarean section and found the transplanted ovary in the same position but flattened out like a pancake and about 8 cm. in diameter. He was able to insert five fingers through this thin ovary into the uterine cavity. Hence his fears concerning a rupture of the uterus were well substantiated.

COMMENT

A great variety of opinions were expressed in the questionnaires. Most of the replies condemned both salpingostomy and tubal implantation, but some approved of both. A few individuals favored salpingostomy and condemned tubal implantations, while others expressed themselves vice versa. The following are representative opinions expressed in answer to question No. 7: "Do you believe salpingostomies and tubal implantations are useful operations? If not, why not?"

Aldridge—"... any technic which restores patency has value from two standpoints. There is always the possibility of pregnancy and the patient's hope for a pregnancy is restored—which forestalled an imminent divorce in the case reported. . . ."

Bland—"Very little value" (Bland has performed more than 100 salpingostomies and 5 or 6 tubal implantations).

Cooke—"A justifiable operation if desire for pregnancy justifies risk, disability and expense of operation in face of rather long odds against success."

DeLee—"My own experience is small and discouraging, but I believe the operations are worth discussing and occasionally deserve practicing."

Dickinson—"Salpingostomy has successes too infrequent to warrant laparotomy for cure of sterility. I checked on Polak's large series and while he at one time advocated it, he later condemned it as useless. Tubal implantation is much more promising."

Frank, R. T.—"Most closures of tubes are due to inflammation. After operation the inflammatory process recloses the tubes."

Farrar—"Yes, decidedly."

Gellhorn (reported by Emmert)—"It is, after all, a matter of individual judgment whether or not the tube appears to be in good condition capable of restoration of function."

Holden—"Yes, if male and female are found to be otherwise normal and if done by a technic similar to that of Sovak."

Kennedy, J. W.—"I can answer in the negative as I feel many of these operations will fail, pregnancy will rarely follow and many patients will return for a second operation."

Litzenberg—"Yes, because they occasionally result in pregnancies. My one success makes me believe it worth while to have done the many unsuccessful operations."

McGlinn—"I am not justified in view of the various risks and the slight possibility of success in urging the operation to be done."

Masson—"I practically never advise the operation and only do it when the patient insists on something of the kind being done."

Mathieu—"I am terribly skeptical about the success of salpingostomy and tubal implantations."

Matthews—"They should really be used more often than they are—which I believe is due to the inability of most operators to perform these operations in a satisfactory manner."

Meaker—"I do not consider that tubal implantation is a justifiable procedure. I believe that salpingostomy is warranted."

Nicholson—"Possibly useful but results reported have been so uncertain that I have not been interested in the subject."

Norris—"Yes, in a certain small group of cases, I believe they may have a place in the treatment of sterility."

Phaneuf—"I personally advise against operation if the decision is left to me."

Rongy—"Spontaneous resolution is likely to take place in a greater number of cases without any operative interference—a negative result after an operation means permanent sterility."

Schmitz—"These operations are justifiable when the patient insists on having offspring, if possible."

CASE REPORT

A case in which I performed both a salpingostomy and a tubal implantation is cited below. The patient subsequently became pregnant twice, once in the uterus and the second time in the implanted tube.

Mrs. F. K., aged twenty-six years, was referred to me by Dr. B. Turman because of sterility. She had been married seven and a half years and had never been pregnant. The husband's semen had been found to be normal. The patient's past history presented nothing abnormal and the menstrual cycle had always been fairly regular and normal. The patient was short and thin. Her general examination and Wassermann reaction were negative. On bimanual examination it was found that there was a normal marital outlet, the cervix was smooth and clean, the fundus was normal in size, hard, anteflexed and movable, the left adnexa felt normal but the right ovary was slightly but definitely enlarged and cystic. A Rubin tubal patency test was performed but the tubes were found to be closed. Two days later hystero-graphy was done, using lipiodol. Fluoroscopic and x-ray examinations revealed a hydrosalpinx on the right side, with numerous beads of lipiodol inside the right tube. The tube on the left side was blocked at the cornual end. The condition was explained to the patient, but she had previously heard a good deal about operations on the tubes and wanted such an operation performed. On Nov. 23, 1932, she was operated upon at the Woodlawn Hospital. Because of the hydrosalpinx on the right side, the distal two-thirds of this tube were removed, the proximal one-third incised almost its entire length, and the tubal mucosa of this portion sewed to the serosa with interrupted fine catgut. Air was blown through the opening thus made into the uterine cavity with a Luer syringe, proving that this small tube was patent. There was a block at the uterotubal junction on the left side. This area with almost one-half of the proximal part of the tube was removed. The distal portion of the tube was then implanted into the uterine corner in the manner of implanting a ureter into the bladder. Air blown through this newly made opening into the uterus went through very easily. The right ovary was found to consist almost entirely of a chocolate cyst. It was removed, as well as the appendix. The postoperative course was entirely uneventful.

On Dec. 16, 1932, twenty-three days after the operation, a tubal patency test was performed which showed that the gas went through the tubes very easily. This test was repeated four weeks later and again the gas went through with a pressure of less than 70 mm. Hg. In June, 1934, the patient missed a period and Dr. Turman had an Aschheim-Zondek test performed which proved positive. On July 3, 1934, the patient had a miscarriage. She was advised to wait at least three months before attempting another pregnancy, but failed to do so. On Aug. 29, 1934, she fainted and began to bleed vaginally. Her last menstrual period had begun on July 17. Examination revealed dark blood in the vagina, a soft cervix, the body of the uterus slightly enlarged, not softened, except in the isthmus, and pushed over to the right side by a soft, cystic, slightly tender, irregular mass which

was presumably adherent to the uterus. A diagnosis of left ectopic pregnancy was made and operation advised. Laparotomy at the Chicago Lying-In Hospital (August 29) revealed a dark, almost black, irregular mass about 5 cm. in diameter protruding from the left uterine corner. The left tube, the one which had been implanted into the uterus, extended out from the dark mass. Its fimbriated end was perfectly normal. It appeared as if the mass had separated explosively the tube from the uterus. The left ovary measured about 8 by 6 by 6 cm. The small right tube was entirely covered over with peritoneum. The uterus was only slightly enlarged, slightly softened, anteflexed, and movable. The ectopic pregnancy was removed together with the left tube. Since the left ovary was the only one the patient had, almost 20 c.c. of serous fluid were aspirated from it and the ovary was left in situ. Knowing how anxious this patient was for a baby, a second salpingostomy was performed on the right tube. The patient left the hospital nine days after the operation.

Gross and microscopic examination of the specimen removed showed an early pregnancy. The villi were typical of those present in the first trimester of pregnancy. The patient was advised to avoid conception for at least one year. Three tubal patency tests were performed after the second operation, the last one on Jan. 28, 1936, and the remaining tube was found to be patent on each occasion.

This patient, therefore, had both an intrauterine and an ectopic pregnancy following a plastic operation on the tubes. Since the tube on which the salpingostomy had been performed was found to be entirely occluded, the pregnancies were made possible by the tube which had been implanted into the left uterine corner.

CONCLUSIONS

A review of the literature concerning salpingostomy and tubal implantation for the purpose of overcoming sterility does not present a favorable picture for these operations. The chief reasons for this are the relatively few live babies secured by these measures, the disproportionately high number of ectopic pregnancies which have resulted, and other complications which may follow such operations.

Questionnaires sent to members of the American Gynecological Society and the American Association of Obstetricians, Gynecologists and Abdominal Surgeons elicited the information that more than one-half of these specialists (60) who answered the questionnaires (107) were definitely opposed to salpingostomies and tubal implantations for the purpose of overcoming sterility, about one-fifth of the individuals were distinctly in favor of such plastic operations, one-seventh felt the operations were worth while occasionally, and the remainder did not express any opinion concerning the usefulness of these operations.

An analysis of about 818 plastic operations reported in the questionnaires revealed that 54 pregnancies took place after these operations, an incidence of 6.6 per cent, or one pregnancy for every 15 operations. However, since there were only 36 live babies delivered, the incidence of a successful result was only 4.4 per cent or one baby for every 22.5 operations. Ten of the 54 pregnancies (18.5 per cent) ended in abortion and 8 (14.8 per cent) were ectopic pregnancies. Hence only 66.7 per cent of the 54 pregnancies resulted in live children.

Careful selection of cases and improved technic of performing these plastic operations on the tubes will most likely yield a larger incidence of live children for those who feel inclined to perform these operations. There is certainly much more justification for doing them when the abdomen is opened for some specific indication, such as chronic appendicitis, ectopic pregnancy, or the removal of an ovarian cyst, than there is for performing the laparotomy solely for the purpose of operating on the tubes to correct sterility.

The following conditions should be present before a plastic operation on the tubes is performed: The patient must be in the childbearing period, preferably under thirty-five years of age; she must have at least one functioning ovary; both tubes or the only tube present must have been proved closed; there must be no other cause for sterility than tubal closure; there must be no gonorrheal, postabortal, puerperal or tuberculous infection in the genital tract, and the patient must be a good surgical risk. Of course, the husband must be fertile and healthy.

I wish to thank those who were kind enough to devote their time and energy in answering my questionnaires.

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55 E. WASHINGTON STREET

NEPHROSIS IN PREGNANCY

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THE term "nephrosis" as used in this report designates a degenerative renal lesion as distinguished from an inflammatory one. To make that simple statement, however, does not convey an adequate concept of what the nephrotic syndrome consists of clinically. The following findings have quite generally been accepted as prerequisite to a diagnosis of nephrosis: marked generalized edema; normal blood pressure, nonprotein nitrogen, and kidney function tests; high blood cholesterol and total lipids; low serum protein and albumin-globulin ratio (latter frequently reversed); marked albuminuria; urinary casts and red blood cells not increased above normal; and the presence of doubly refractile cholesterol ester bodies in the urine. At autopsy the kidney tissue should show no inflammatory but a degenerative change involving principally the tubules.

Any condition whose characteristics can be so specifically postulated would on first thought seem easy of diagnosis. The difficulties encountered, however, are indicated in the following statement by Dunn, "Vollhard from a wealth of experience has acknowledged that amyloid nephrosis and subacute nephritis alike may be indistinguishable by any criterion from simple chronic nephrosis during life, a conclusion also arrived at by Leiter from an exhaustive survey of the literature on this subject."

The observed facts which form the basis for this conclusion by the two recognized authorities just mentioned have led others seriously to

question the existence of nephrosis as an entity. Thus Christian says, "Nephrosis is the name of a clinical syndrome, but is the name of neither a disease nor of a definite pathological lesion." Likewise Blackman, "Nephrosis is a particular form of diffuse nephritis—," and Bell, "Lipoid nephrosis is not a distinct entity but a form of glomerulonephritis." In response to these last opinions, Leiter acknowledges that in its primary uncomplicated form nephrosis is a rare disease and then quite pertinently reminds that its rarity is, however, no justification for the denial of its existence. No attempt will be made here to credit or discredit the views of either side of this controversy.

The sole purpose of this writing is to place on record three cases that in the minds of those who studied them seemed to satisfy the conditions that would make a diagnosis of nephrosis acceptable. These three cases were among approximately twelve thousand obstetric patients admitted to the same service over a period of nine years. This gives an incidence of 0.025 per cent. The fact that these patients were all pregnant when first seen may have some significance in relation to the repeated observations of others that in certain cases the onset of nephrosis appears to be definitely associated with pregnancy, or in cases where a diagnosis is made prior to pregnancy the condition is aggravated greatly by pregnancy.

Brief case histories are submitted.

CASE 1.—E. L., white, gravida i, aged twenty-two, due May 27, 1927. Admitted to hospital Jan. 14, 1927, because of generalized edema. Significant findings on admission: pallor, general anasarca, double hydrothorax, ascites, edema of retinae, blood pressure 128/82. Marked albuminuria, casts (granular and hyaline), low plasma protein. During three and one-half weeks in hospital on high protein, restricted salt diet, there was marked clinical improvement and patient was discharged for observation in O.P.D. Admission weight 148, discharge weight 118. Alb. 4 gm/L—19 gm/L.

Readmitted Feb. 27, 1927, following spontaneous rupture of membranes and onset of labor. Delivered of macerated stillborn fetus. Edema very greatly improved. Blood pressure normal. Albuminuria persistent. Blood findings: anemia and low protein. In hospital four and one-half weeks. Admission weight 122, discharge weight 115. Alb. $4\frac{1}{2}$ gm/L—11 gm/L. Sterilization recommended, refused.

Readmitted to hospital June 13, 1927, eight weeks pregnant. Edema of lower extremities. Albuminuria. Therapeutic abortion by hysterotomy and sterilization by tubal resection done. Uneventful recovery. Blood pressure normal.

Seen at irregular intervals during the following seven years. Subjectively had little complaint until four years had passed. Then began complaining of headaches and dependent edema. Urine constantly showed albumin.

Admitted to hospital again October, 1934, because of very marked edema, dyspnea, vomiting, and weakness. A severe anemia was also present at this time for which a transfusion was given. Cystoscopic examination showed a marked cystitis and pus coming from the right ureter. Hypertension and nitrogen retention were two important findings at this time. Left hospital under protest. Died within the next two months. Was not seen after last hospital admission. No autopsy. Laboratory details in table.

CASE 2.—I. McL., white, aged twenty-nine, gravida ii, para i, first seen in O.P.D., Jan. 19, 1932, at approximately thirty-two weeks' gestation. Came to Clinic because of marked edema of lower extremities and dyspnea for past four months. Admitted directly to hospital. History of similar course in first pregnancy two years prior, at which time she was induced at eight months, because of "kidney and heart disease." Following this delivery her symptoms disappeared promptly and she felt well. Had felt well for ten years prior to her marriage and first pregnancy at age of twenty-seven. Admission findings were: mild gingivitis, few râles in right base posteriorly, marked edema of lower extremities, with pitting to well above the knees. Blood pressure 130/85. Urine boiled solid and showed granular casts. After forty-eight hours in hospital the casts were reduced to just occasional occurrence and after the tenth hospital day no more casts were demonstrated although daily specimens were examined throughout the hospital stay. Doubly refractile bodies were constantly present in the urine.

Following complete laboratory study it was considered this case best could be classified under a diagnosis of nephrosis for the following reasons: Long history without progression, intermittency of edema, negative eyegrounds, marked albuminuria, absence of blood and casts (excepting appearance of latter in first urines following admission). Low basal metabolism rate, normal blood pressure, normal kidney function tests, low serum protein, high total lipids, decreased and reversed A/G ratio and constantly present doubly refractile bodies in urine.

Accordingly patient was placed on a high-protein, low-salt diet. Repeated basals showed -7, -7, -4 per cent.

Thyroid administration did not appreciably change the condition. The edema varied in amount from time to time, involving chiefly the most dependent portion of the body and influenced definitely by posture in bed. Edema of the labia occurred. Albuminuria varied from 3 to 15 gm/L during the hospital stay.

At approximately the thirty-seventh week, the labial edema made the patient very uncomfortable and consequently a medical induction with castor oil and quinine was attempted successfully. She was delivered of a 3,030 gm. living child. Following delivery there was immediate and marked improvement. The water balance previous to delivery was consistently positive, intake being restricted to between 1,500 and 2,000 c.c. Following delivery this was reversed and the urinary output exceeded the fluid intake for 7 consecutive days. Just before delivery the patient weighed 114 pounds. Eleven days postpartum she weighed 90 pounds. On discharge the twentieth day, postpartum, she weighed 94 pounds. Changes in the laboratory findings are noted in Table I.

In the three-year period following her second delivery this patient was seen on 3 different occasions: four and one-half months, fifteen months, and 40 months, postpartum. Subjectively she has had no complaints in this time and is doing all her own housework. The laboratory findings for this follow-up period also appear in the table. Reported as well and working hard March, 1936.

CASE 3.—J. T., first pregnancy at seventeen years of age, in 1930. Observed from October 3 to delivery on February 14 (8 clinic visits). In hospital from Oct. 8, 1930, to Oct. 10, 1930, because of blood pressure of 158/72 and 155/70 on first two clinic visits. Two blood chemistries, normal figures. Phenolsulphonephthalein normal, blood pressure not over 130/80. Discharged in two days to out-patient department. Blood pressure below 130 for next two clinic visits, then up to 140 and 150 again. No albumin.

Admission to hospital in labor Feb. 14, 1931. Blood pressure 148/80. Albumin plus. Delivered after sixteen hours labor of a 3,500 gm. living infant. Discharged twelve days postpartum. Blood pressure 120/80. Faint trace of albumin.

TABLE I.—NEPHROSIS

CASE	AGE	GRAVIDA	SYMPTOMS	TREATMENT	WEIGHT MAX. MIN.	GEST.	TERMINATION
I E. L.	22 yr. Jan., 1927	i	General anasarca. Hydrothorax, bilateral edema of retinae. Pallor. Albuminuria	Bed rest. High protein, salt poor diet	148	118	23 wk.
	Feb., 1927		Spont. rupture with onset of premature labor		122	115	30 wk. Still-birth
	June, 1927	ii	Edema of lower extremities. Albuminuria	Therapeutic abortion. Sterilization			8 wk. Abortion
	Feb., 1929		No complaints				
	Mar., 1932		Dependent edema				
II I. McL.	29 yr. Jan., 1932	ii	Generalized edema. Dyspnea. Dizziness. Spots before eyes	Bed rest. High protein, salt poor diet. Thyroid	114		32 wk.
	Feb., 1932		Edema increase	Same	122		34 wk.
	Delivered February						3030 gm. living child
	Mar., 1932		No edema. Subjectively well	High protein, low salt diet		95	20 da. p. p.
	May, 1933		No complaints	Unrestricted diet	98		15 mo. p. p.
III J. T.	21 yr. Jan., 1934	iv	Marked generalized edema. Palpitation. Dyspnea	Bed rest. High protein, salt poor diet. One blood transfusion. Two blood plasma infusions	197		16 wk.
	Mar., 1934		Anasarca. Edema of labia. Backache	Bed rest. High protein, salt poor diet. 150 gm. acacia in glucose I. V. in 5 da. period. Whole blood transfusions. Additional 90 gm. I. V. acacia. Anti-strep. serum.	189 192		23 wk. 24 wk.
						180	2 da. p. p.
			Delivered April 11, 1934.				
			Died April 17, 1934.				

*100% = 13.8 gm.

Second pregnancy. Aged nineteen, 1931. Observed from May 5, 1931, to delivery on Sept. 13, 1931. Blood pressure 138/74. Delivery spontaneous after eight hours of a 3,200 gm. living infant. Discharged eleven days postpartum. Blood pressure 125/75. No albuminuria at any time in association with second pregnancy.

Third pregnancy. Aged 20, 1933. Observed from January 24 to delivery on April 1 (6 clinic visits). Urine showed no albumin prenatally. Blood pressure ranged from 140/70 to 160/80. Admitted to hospital in active labor Apr. 1, 1933. Blood pressure 150/74. No albumin. Delivery after fifteen hours labor; 3,600 gm. baby, living. After delivery blood pressure never over 130 systolic. Had been on pre-eclamptic diet for six weeks before delivery. Discharged on eighth day postpartum.

Fourth pregnancy. Aged twenty-one, 1933. Came to clinic twelve weeks pregnant. Last menstrual period October 2. Estimated date July 9. Admitted to hospital for study. Shortness of breath, fatigue, palpitation, and marked edema since onset of pregnancy. Diagnosis of nephrosis based on: (1) Normal kidney function tests,

IN PREGNANCY

BLOOD PRES- SURE	EDEMA	URINE				BLOOD					
		ALBUMIN	CASTS	R. B. C.	DOUBLY REFRACTIVE BODIES	*HB. %	SER. PROT. GM. %	CHOL. MG. %	N. P. N. MG. %	TOTAL LIPID MG. %	A/G RATIO
128/82	Generalized, marked	4-19 G/L	Hyaline	0	Present	67	3.1	560	30		1.0
120/65 110/50	Mild	4.5-11 G/L	Hyaline	+	Present	59	3.4	375	30		
120/60 110/55	Mild	4-6 G/L	0	0	Present	75	3.1	466	37		
	None	4 G/L	0	0	Present	95	4.8	198	38		
	Mild	5 G/L	Hyaline	0	Present	89	5.5	390	89	903	
	Marked	6½ G/L	Hyaline Granular	+	Present	43	5.3	256	200	1170	1.14
130/85	Marked	6 G/L	Granular Hyaline	0	Present	77	4.0	400	27	1194	1.26
135/90	Marked	5 G/L	0	0	Present	74	4.0	364	27	1179	0.8
125/85	None	5 G/L	0	0	Present	86	4.4	372	35	969	1.23
130/85	None		Hyaline	0	Present	105	5.3	400	29	528	3.3
135/85	None	3 G/L	0	0	Present	95	5.8	375	20	677	
110/65 to 140/90	Marked	6-12 G/L	0	0	Present	88 105	4.6 5.6	552 720	18 26	1875	0.65 1.0
135/80	Marked	13 G/L	0	0	Present	3-12-34 91	4.5	727	28	1930	0.77
128/70	Marked	8 G/L	0	+	Present	3-17-34 77	3.9	485	31	1462	0.84
135/75	Marked	10 G/L	Hyaline Granular	+	Present	4-13-34 80	3.3	640	53	1255	

(2) normal blood pressure, (3) absence of casts and R.B.C. from urine, (4) albuminuria, (5) low serum protein, (6) A/G ratio less than 1, (7) high cholesterol and total lipids, (8) doubly refractile bodies in urine, and (9) normal eyegrounds.

Placed on high protein (2 or 3 gm. per Kg.), low salt diet. Weight decreased from 197 to 165 pounds (32 pounds) in first twenty-nine days in hospital. Still was not entirely edema free when she began gaining weight again.

In the next ten days she gained 11 pounds. As diet alone failed to relieve symptoms, patient given 675 c.c. citrated whole blood. Crying spell with rubbing of eyes resulted in so much edema of lids that patient could not see.

Hemoglobin after transfusion 105, blood serum protein still low so patient was given 275 c.c. blood plasma and 375 c.c. of blood plasma eight days apart. Continued to have low serum protein and tendency to regain some of the weight recently lost, although in general the clinical picture was one of improvement. At this time patient demanded release from hospital because of illness of her mother. Accordingly released under protest with instructions as to diet, rest and elimination.

During this hospital stay daily blood pressure reading ranged between 110/65 and 140/90, most at level of 125/70. Albumin varied between 6 and 12 gm/L. I.V. Phenolsulphonephthalein 80 per cent in two hours. Urea clearance 105 per cent normal. Creatinine excretion test: first hour 45, second hour 179, third hour 100.

After seven days at home she re-entered the hospital with marked edema that made it impossible for her to stay on her feet. In the preceding forty-eight hours there had occurred a tremendous edema of the labia. In the seven days at home she had gained 12 pounds in weight.

Elevation of foot of bed to relieve dependent edema resulted in shift of edema to upper trunk and consequent difficulty of respiration with coughing and some blood-tinged sputum. Within a few hours after leveling the bed, the labia began increasing in size again. Multiple punctures were made to relieve the painful tension in the labia which was very troublesome because the only position that the patient could maintain for more than a few minutes at a time was flat on her back with the thighs in wide abduction.

Since both diet and transfusion of whole blood and plasma failed to relieve the edema, the patient was given acacia solution intravenously. She received 500 c.c. of 6 per cent acacia in 20 per cent glucose for five successive days. (Total of 150 gm. acacia.) On the day the acacia was started the hemoglobin was 98, five days later it was 71. Then given whole blood transfusion of 650 c.c. One week later given 350 c.c. whole blood. Two days later given 750 c.c. whole blood. Hemoglobin back then to 87. Five days following the last transfusion and after fourteen days during which the q four hour temperature record showed no temperature over 37.4° C. the patient suddenly complained of chilling and temperature rose to 40.8° C. Lungs were clear. The following day patient went into spontaneous premature labor and delivered a twenty-seven-week-old living male infant, 1,100 gm., which lived 6 days. Two days following delivery, patient complained of generalized abdominal pain. Lungs clear. Abdomen markedly distended, central part resonant but dullness in flanks. Impression was: Free fluid in abdominal cavity, probably infected. Paracentesis considered but deferred. Given 650 c.c. of whole blood. Blood culture positive showing a gram-positive hemolytic streptococcus. Following day she was given 500 c.c. of 6 per cent acacia in 20 per cent glucose and 20 c.c. of antistreptococcus serum. That evening she was given 650 c.c. of whole blood and another ampoule of antistreptococcus serum. Following day 500 c.c. of 6 per cent acacia in 30 per cent glucose and 20 c.c. of antistreptococcus serum were given. Later same day given 700 c.c. citrated whole blood and 20 c.c. antistreptococcus serum. Following day was given 6 per cent acacia twice in glucose. Died Apr. 17, 1934.

The organisms cultured from the blood stream were gram-positive hemolytic streptococci that grew best anaerobically. Organism cultured from peritoneal cavity at autopsy, gram-positive hemolytic streptococcus.

Autopsy report: Nephrosis, fatty liver, peritonitis, hydrothorax and hydro-pericardium, and septic spleen.

DISCUSSION

CASE 1.—E. L. The marked daily loss of urinary albumin, 4.5 to 11 gm. per liter, made it especially interesting to know more about the N balance of this patient. Peters, Bulger and others have shown by complete studies in nephritis that the urinary N, while it does not represent all the N lost, is still an index of body catabolism. Table II gives the results of metabolism studies on this patient over a period of twenty-three consecutive days immediately following her first hospital admis-

sion. Fluids were not limited although the intake was never great. Diuresis was marked and prolonged. The NaCl output was rather low, the level of excretion usually falling between 0.1 per cent and 0.4 per cent. A marked albuminuria was persistently present. It is significant that this was uninfluenced by diet. There were wide variations in the albumin content of different specimens, the average falling at approximately 0.5 per cent or 5 gm. per liter. The specific gravities of the urines varied between 1.022 and 1.006 with an average of 1.011. The N intake and output were about equal for the duration of the test.

TABLE II. METABOLISM STUDIES ON CASE 1 DURING FIRST HOSPITAL ADMISSION. FIGURES REPRESENT AVERAGES FOR FOUR CONSECUTIVE FIVE-DAY PERIODS

DATE	LB. WEIGHT	C.C. FLUID INTAKE	C.C. URINARY OUTPUT	ALBUMIN %	ALBUMIN GM./24 HR.	NaCl %	NaCl GM./24 HR.	TOTAL N OUTPUT	TOTAL N INTAKE	N BALANCE
1927										
Jan. 15 to 19 incl.	144.3	1,086	1,775	0.66	10.4	0.34	5.7	7.6	6.0	-
20-24 incl.	137.5	1,145	1,576	0.60	9.2	0.32	5.1	6.2	6.9	+
25-29 incl.	127.6	1,016	2,296	0.62	14.3	0.36	8.46	8.1	7.9	-
Jan. 30 to Feb. 3 incl.	118.9	1,530	1,572	0.65	10.3	0.38	6.1	7.4	7.7	+

This patient promptly showed a definite increase in edema and albuminuria from the onset of the second pregnancy. While the edema disappeared following the abortion, the albuminuria never entirely cleared. During the last three years of her life there was a gradual but certain rise in blood pressure and in the last few months a degree of hypertension and nitrogen retention that established the terminal condition as one of chronic nephritis.

CASE 2.—I. McL. Unfortunately, we have no observations on this patient in her first pregnancy. After the complete study made in the latter part of her second pregnancy, however, it would seem quite apparent that the unfavorable signs and symptoms observed then were simply a repetition of what occurred also in her first pregnancy, and that the original diagnosis of "kidney and heart disease" resulted from a misinterpretation of the etiology of the generalized edema and marked albuminuria noted by the attending physician at that time. The points of particular interest in this case are that she was able to carry on in what she considered a perfectly normal manner when not pregnant, that the onset of a pregnancy each time was immediately associated with the unfavorable signs noted in the history, that these signs became progressively worse to the point where they demanded early induction of labor, that prompt relief of the subjective symptoms followed delivery, and that the patient continues to be free from any subjective complaints. She is now in her fifth year since her last delivery.

CASE 3.—J. T. This patient was observed through three pregnancies before developing her serious difficulty in the fourth. She showed an occasional tendency to mild elevation of blood pressure. There was never any nitrogen retention and each time there was a prompt return of blood pressure to normal on bed rest. No hypertension was ever noted postpartum. From the very onset of the fourth pregnancy edema was a prominent feature, in fact was the reason for the patient's coming to the clinic in her twelfth week of gestation. As soon as the nephrotic character of her difficulty was recognized, an attempt was made to raise the level of her blood protein and to reduce the edema. High protein diet, whole blood transfusion, blood plasma infusion and gum acacia infusion were used. The initial response to forcing 2 or 3 gm. of protein per kg. of body weight and restricting salt at bed rest was favorable, particularly in reducing the edema, but later became quite ineffective. There was no appreciable effect on the level of the blood protein. For this reason a whole blood transfusion, 675 c.c., was given, following which the hemoglobin was found to be well over 100 per cent with the total proteins still low. This was the indication for the blood plasma infusions which, however, also failed to improve the total protein level. It was very unfortunate that the illness and death of the patient's mother at this point caused her to demand release from the hospital, for on her return seven days later, she was more edematous than at any time previously. Since diet and infusion of both whole blood and blood plasma failed to improve the condition, it was now decided to try the effect of intravenous gum acacia. Hartmann has reported good results from the use of acacia in the treatment of nephrosis in children. The amount of acacia given to this patient was not as great, calculated on the basis of body weight, as was found necessary to produce satisfactory results in some of the patients treated by Hartmann. A moderate increase in urinary output with corresponding decrease in edema followed the use of acacia, but the serum protein dropped to even lower levels than had been present before. Since the passing of this patient, there has been reported the successful treatment with intravenous acacia of a case of nephrosis in an adult woman by Barach and Boyd. Their patient was twenty years of age, was given 295 gm. of acacia intravenously over a period of four weeks following which she was discharged as "cured." She remained well under observation for one and one-half years after the acacia treatment and then went through an uncomplicated pregnancy. The untimely death of our patient resulting from an acute streptococcic blood stream infection and peritonitis of unexplained origin precluded the possibility of further observation and estimation of the value of the acacia treatment.

Each of these three cases of nephrosis in pregnancy has followed a different course. The first passed over into a chronic nephritis which proved fatal seven years after the patient first came under observation:

the second carries on in a manner quite satisfactory to herself until she becomes pregnant when the typical picture of nephrosis presents itself in constantly increasing severity until relieved by delivery; the third succumbed to a peritonitis of unknown origin. Other writers have called attention to this same triad of fates any one of which may be the lot of these unfortunate individuals. The patient in Case 2, still living, represents that group that may live for an indefinite period of years until finally carried off by some intercurrent infection.

The effect of pregnancy on nephrosis is very interesting and particularly significant in the light of the observation that repeated reports definitely link the onset of the condition with a pregnancy. The significance of this lies in the fact that even in normal pregnancy certain changes occur in the kidney which simulate the changes noted in nephrosis, and which for want of a better term have been designated as "the kidney of pregnancy." It requires no great stretch of the imagination to picture the possibility of an individual with a nephrotic tendency becoming pregnant and then under this double influence (in an unfavorable direction) developing the typical clinical syndrome of nephrosis. It is also quite possible that in certain susceptible individuals the nephrotic tendency initiated by pregnancy alone may develop to such a marked degree during the course of the pregnancy that the typical clinical picture of nephrosis results and persists even after delivery has occurred. Viewed in this light pregnancy must be considered as carrying a very real hazard for the woman with a known nephrosis or nephrotic tendency.

One of the chief difficulties met in the management of these cases is to keep the protein intake at a satisfactorily high level. All three of these patients tired very quickly of the prescribed high-protein, salt-poor diet. No doubt an important factor in this anorexia is the withholding of salt.

One more point should be covered in conclusion and that is the question of casts and red blood cells in the urine. It will be seen from Table I that two of these patients from time to time showed casts and red blood cells. Addis has proved that normal individuals, if studied consistently, will excrete these formed elements, sometimes in quite large numbers. Goldring, reporting in 1931, considered the excretion of 500,000 R. B. C., and 5,000 casts per twelve hours, as normal. More recently Elden and Cooney in working with the Addis count in pregnancy found that the excretion of casts and red blood cells in normal pregnancy is greater than the values accepted up to the time of their report (1935) for normal nonpregnant individuals. It becomes obvious then that if any significance is to be placed on the presence of casts and red blood cells in the urine, they must be excreted *in excess* of the number found in normal individuals. Also the finding of Elden and Cooney that preg-

nant women have a higher excretion level of these elements than non-pregnant women is pertinent to this report in that all three of these patients were pregnant when the studies were made.

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MALIGNANCIES OF THE VULVA

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OF 27,380 patients seen in the Women's Clinic of the Stanford School of Medicine between 1918 and 1935, 413 or 1.5 per cent were afflicted with malignancies of the genital organs, with a primary seat of origin in the vulvar region in 20 or 4.8 per cent. Although this disease is relatively common, the literature which has accumulated on this subject since Morgagni gave the first accurate account in 1751 is not extensive.

Europe has contributed the greatest number of records of this disease, and collected statistics of importance may be found in contributions by Mayer,¹ Dittrick,² Bell,³ Rothschild,⁴ Basset,⁵ Ederle,⁶ and Kehrer.⁷ American statistics are comparatively meager. Taussig⁸ recorded the data of 76 cases of vulvar carcinoma seen by him over a period of twenty-two years. Rentschler⁹ reported 71 cases of epithelioma of the vulva seen at the Mayo Clinic between 1907 and 1927. Stein,¹⁰ Noble,¹¹ Reid,¹² Brady,¹³ Massey,¹⁴ Broders,¹⁵ and Goforth¹⁶ have added case reports to the earlier literature.

It is generally agreed that vulvar malignancies are best divided according to their frequency of occurrence, into (1) carcinoma, (2) sarcoma, (3) embryonal tumors, (4) melanoma, and (5) metastatic tumors, as chorioepithelioma or hypernephroma. Of these, only carcinoma is fairly common. Taussig⁸ suggests that the latter should again be subdivided according to frequency and location, into epidermal cancer, cancer of the clitoris, vestibular cancer, and cancer of bartholinian gland. According to location, the twenty cases seen by us group themselves as follows: labia majora 8, prepuce 3, labia minora 2, combined types 5, bartholinian gland 1, and urethra 1.

Kehrer,⁷ who collected 910 cases of cancer of the vulva from the German literature, found that 40 per cent occurred at the labia majora, about 15 per cent at the labia minora, 17 per cent at the clitoris, 0.2 per cent in bartholinian gland, and the remaining 27.8 per cent were of the vulvourethral, fourchette, or combined types. While there are differences in the percentage of location according to size of series reported, it is evident that the labium majus is the commonest site of occurrence.

Malignancy of the vulva rarely occurs before late middle and old age. In Rothschild's⁴ tabulation of 331 cases, the incidence was greatest in the sixty- to seventy-year group. It very seldom occurs in young women. In our series, 3 occurred in the fourth decade, 4 in the fifth, 2 in the sixth, 7 in the seventh, 3 in the eighth, and one in the ninth.

Cancer of the vulva is very frequently preceded by leucokraurotic changes (Graves and Smith,¹⁷ and Taussig⁸). Since there seems to exist a relation between cessation of ovarian activity and leucoplakia and kraurosis, the former may constitute an etiologic factor. Eight of our patients showed definite leucoplakia of the vulva at the time malignancy was discovered. The relative frequency of malignancy in the region of the clitoris and prepuce has been attributed to the common occurrence of leucoplakia in this location. Often both of these structures are involved, and the site of origin is not easily determined. Only about 14 per cent of all cancers of the vulva occur at the vestibule (Taussig,⁸ Kehrer⁷), where leucoplakia is less common.

It is of particular interest that Taussig⁸ found that eight of his ten cases of vestibular cancer originated in the margins of syphilitic ulcers. We found a similar occurrence in a white woman, who, according to an undisputed microscopic diagnosis, had a carcinoma of the labium majus which cleared up under antisyphilitic treatment. Vulvar carcinoma is rare in negroes. Taussig¹⁸ observed only three, and two of these, also, occurred in the margins of tertiary syphilitic lesions of the vestibule. In our series, there was only one negro.

Trauma has been mentioned as a predisposing factor (Kehrer⁷). Multiparity, however, cannot be considered as a factor, since many cases have occurred in nulliparous women. According to Ewing,¹⁹ the incidence of traumatic tumors is found to be extremely low. A single trauma of normal tissues, according to most pathologists, is incapable of producing a malignant tumor. Repeated trauma to successively altered tissues is more likely to cause malignant changes than is a single injury. That injury usually accelerates the growth of tumor cells is not supported by experimental and clinical evidence.

Primary cancer of bartholinian gland develops as a subdermal tumor and is most often an adenocarcinoma. Whenever such a cancer is made up of squamous cells, it has arisen from the epithelium of the ducts (see Fig. 1). Infection apparently plays no important rôle in

its etiology. The incidence of carcinoma of the bartholinian gland is insignificant when compared with the common occurrence of infection of this structure. The case of cancer of bartholinian gland reported here was of the squamous cell variety, and there was no history of previous infection in this instance.



Fig. 1.—Epithelioma of bartholinian gland duct (low power).

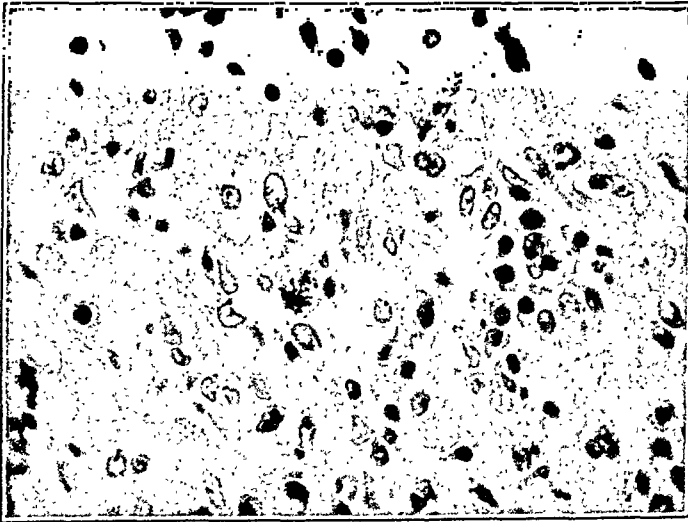


Fig. 2.—Sarcoma of urethra. (Mitosis.) (High power.)

Up to 1913, Rothschild⁴ found only 35 cases of sarcoma of the vulva reported in the literature. This type of tumor is seen most often in younger patients. Its common site of origin is the labium majus. Kelly²⁰ reported one case of myxosarcoma of the clitoris. We have observed one mixed-cell sarcoma of the urethra or periurethral region (see Fig. 2).

As far as could be ascertained from the literature, only 3 cases of teratoma of the vulva have been reported. All of these occurred in very young children. Ley²¹ reported the presence of such a lesion at birth, which was characterized by rapid growth and ulceration.

Metastatic tumors of the vulva are very uncommon. The first report of metastatic chorionepithelioma of the vulva was made in 1895 by J. Whitridge Williams.²² In 1929 Kehrer⁷ reported one case of metastatic sarcoma, 2 cases of metastatic hypernephroma, and 11 cases of metastatic chorionepithelioma.

Malignant melanomas, which were formerly classed with sarcomas, are now generally grouped with tumors of epithelial origin.

Bell³ found that this type of tumor occurred most often in women past fifty years of age. As far as is known, it always originates in a pigmented mole and metastasizes very early to the regional lymph glands. It is generally agreed that this tumor offers an extremely bad prognosis. Goforth¹⁶ and Holland²³ reviewed 52 cases of melanoma and found that 72 per cent occurred in the sixth decade. All investigators stress the point that pigmented nevi, particularly those of the pubic region, furnish the starting point for this most malignant tumor.

With the exception of the melanomas and sarcomas, a neoplasm of the vulva usually appears as a hard nodule in the skin or the mucosa, simulating an inflammatory lesion. Cancer of Bartholinian gland and of the clitoris most often develops in the subdermal tissue. Contact implants on the opposite labium are a frequent occurrence, and, according to Franke,²⁴ such transplant formation may be the result of (1) invasion by carcinoma through the blood or lymphatic vessels, (2) mechanical irritation of the tumor itself, (3) lowering of the local resistance caused by the secretion of the ulcerated tumor, (4) direct transplantation of masses of cells, and (5) the implantation of the organisms, if organisms can produce carcinoma. Perhaps direct transplantation into a contact area made suitable for implantation because of surface maceration is the most likely explanation.

The symptoms observed in the various types of malignancies of the vulva are fairly uniform, and are characterized by itching, burning, lump formation, ulceration, pain, and dysuria. The discovery of a "lump" was the outstanding complaint in fifteen of our twenty cases. In nine instances, there was an additional complaint of intense itching at the site of leucoplakia. In three instances, burning on urination was the predominant symptom. Bloody discharge was observed by several patients. In the more advanced cases, edema and a radiating pain down the legs were present.

It is sometimes very difficult to differentiate early cancers from leucoplakia. Biopsy is a very important diagnostic procedure in all cases, as any form of chronic hypertrophic or ulcerative vulvitis, chancreoid, or granuloma may simulate cancer of the vulva. Melanomas usually can be diagnosed from the pigmentation present. Syphilitic ulcers may present difficulties in diagnosis, but the Wassermann re-

action and the results of antisyphilitic treatment usually establish the diagnosis. In eighteen of our twenty cases, the diagnosis of malignancy was made clinically.

The cytologic composition of these tumors, to a certain extent, is dependent upon the site of origin. Most of them are epitheliomas, and it is common to find a well-differentiated cell picture of large areas of pavement epithelium with pearl formation (see Fig. 3). In some instances the downward involvement is slight, although the surface proliferation may be great. In such tumors, mitotic figures are infrequent. Certain tumors are characterized by anaplasia and great cell activity, with less differentiation and greater invasion of the underlying tissues. The latter type is most frequently seen in younger patients, particularly if the neoplasm has arisen in a syphilitic ulcer.



Fig. 3.—Epithelioma of vulva, pearl formation (low power).

We have divided our tumors into mature, mid-mature, and immature types, following essentially the classification of Schottlaender and Kermauner.²⁵ Accordingly, "mature" indicates a cell differentiation which approaches that of the normal squamous epithelium. "Immature" indicates a cytologic picture which shows no resemblance to the parent tissue but approaches the cell appearance in the embryonic state. Cell outlines cannot be made out clearly, and nuclei vary greatly in size and shape. Anaplasia is common. The "mid-mature" type occupies a position midway between the other two types, and may vary considerably in cellular appearance.

The treatment of cancer of the vulva should depend upon the extent of the disease and the general condition of the patient. It may consist of surgery or irradiation, or both. The prevailing opinion is

that vulval cancer is best treated by surgery, since it alone offers any appreciable chance for cure, and that irradiation should be reserved either as an adjunct to surgery or as a palliative measure. As a general rule, wide excision of the growth, including the regional lymph nodes, should be the method of choice. It is doubtful that postsurgical irradiation is of value in borderline cases. In advanced cases, the placing of radium needles, followed by roentgen irradiation, may give temporary relief. Local lesions may respond surprisingly well to deep therapy, but as a rule the course of the disease remains unchanged. Whenever leucoplakia is present, removal of the neoplasm should include all of the leucoplakic area. This offers the best protection against further malignant degeneration.

There are various surgical methods for the radical removal of lymph glands.

Basset⁵ advocated a two-stage operation, with a systematic resection of the lymph-glands in the first stage, followed by vulvectomy after the inguinal incisions have healed. The great advantage of this procedure lies in the shortened postoperative course. Stoeckel²⁶ and Kehrer⁷ devised an operation for the removal of the iliac glands in addition to the deep and superficial inguinal glands. This operation carries a primary mortality ranging from 11 to 15 per cent. Taussig,⁸ using a modification of the Bassett technic, reported an operative mortality of only 3.3 per cent. In his opinion, the primary mortality is considerably reduced if intraperitoneal manipulation is avoided.

Janeway and Bailey²⁷ were among the first to employ radium and x-ray in the treatment of cancer of the vulva, but final results have not been reported. In 1926 Heyman²⁸ reported 64 patients who, because of inoperability, were treated palliatively by irradiation. Twenty-one showed no improvement, but for the remaining patients he reported one 7-, one 6-, one 5-, one 4-, one 3-, and five 2-year cures. Collecting 126 patients treated by irradiation, including Heyman's series, Taussig⁸ found only 15 cures of over five years' duration. It would be faulty to compare these results with those obtained in selected operative cases, since many of them were considered inoperable before treatment. Eleven of our cases were considered inoperable and were therefore treated by irradiation. Two of these died soon afterward from other causes (suicide, cerebral hemorrhage). The average duration of life for the remaining 9 patients was sixteen months. One patient lived for two years and four months after irradiation.

Tausch,²⁹ in his review of 47 cases of vulvar carcinoma, reported 24 patients operated upon radically with additional deep roentgen therapy in 8, and a combination of x-ray and radium in 15. In the latter group, only one patient survived five years, but died a few months later from a recurrence. Of the 39 patients treated surgically, with or without postoperative irradiation, 16 remained alive for more than five years.

Taussig⁸ reports discouraging results from irradiation. Of 15 patients treated with deep x-ray and radium, only one survived the three-year period. The poor results are probably due to the high incidence of well-differentiated radium-resistant tumors, the ineffective results of x-ray treatment on inguinal and femoral metastases, or the advanced stage of the growth.

Preoperative irradiation has not been given a sufficient trial to be evaluated. Marcus³⁰ reported two patients in whom operation was preceded by x-ray and radium exposures, and a histologic study of the regional glands revealed no effect from irradiation. He concluded that vulval carcinoma should be treated by radical operation alone.

Patients suffering from *sarcoma* of the vulva or *carcinoma* of the clitoris have, in every instance, in spite of *any* treatment, died very soon after the discovery of the tumor. All cases of operative removal of teratomas of the vulva proved fatal. Epitheliomas, especially those originating in leucoplakic areas, present a more hopeful outlook.

Taussig⁸ reports 81.8 per cent of five-year cures of *operable* cases treated radically according to Basset's technic. On the other hand, Rentschler⁹ believes that the prognosis is fair only for the prolongation of life, but poor for a cure regardless of the type of operation or operation followed by irradiation. Of the 62 patients in his series, 44 died within five years, the average duration of life being two years and one month.

The treatment of melanomas of the vulva by either surgery or irradiation gives uniformly poor results. In Holland's²³ series, most of the patients were dead within six months after operation.

Taussig⁸ and Goforth¹⁶ concluded that all pigmented nevi of the vulva should be regarded as malignant and treated by wide excision with a wide margin of healthy tissue removed in all directions. If any degenerative change has occurred, the nevus, together with the regional lymph glands, should be removed.

SUMMARY

Twenty cases of malignancy of the vulva were studied. Five were treated by radical vulvectomy, and 4 by local excision and irradiation. The remaining 11 patients received irradiation only. Of those treated by radical operation, 3 are still well after three, four, and five years. One patient of the 4 treated by local excision and irradiation remains free from recurrence, and the other 3 died three, six and fifteen months after operation. Of the 11 patients treated by irradiation alone, the longest survival was two years and four months.

CONCLUSIONS

Because of the high incidence of well-differentiated tumors, surgery offers the best chance for permanent cure in vulvar malignancies, provided the neoplasm in question belongs to the operable group. Irradiation is essentially a palliative measure.

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THE TREATMENT OF DYSMENORRHEA*

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THE relief of primary dysmenorrhea has been a baffling problem always. The young woman may have very severe pain, with nausea and vomiting, keeping her in bed for one or more days each month, yet pelvic examination may disclose that the uterus, oviducts, and ovaries are in normal position and of normal size. In some instances a small, firm uterus, the body of which is acutely anteflexed, the hypoplastic type of uterus, is found as the only abnormality.

In earlier days the only advice these patients were given was that pregnancy would bring relief and in case pregnancy was not anticipated or did not occur soon after marriage dilatation and curettage was advised, because the pain was thought to be attributable to obstruction to the escape of menstrual blood. In a number of cases the dysmenorrhea persisted after delivery and in most instances dilatation and curettage gave only temporary relief of pain.

With the advent of various ovarian extracts, and more recently of the hormones, it was hoped that these substances would, in some mysterious way, bring relief to this large group of women who are seriously handicapped by the pain accompanying a normal physiologic function. Perhaps when more is known of the part played by the hormones concerned in the menstrual cycle, the cause of the accompanying pain may be determined and means may be found to relieve it. At present the giving of estrogenic hormones to a patient whose uterus is undeveloped seems to be the only logical indication for use of the hormones in treatment of dysmenorrhea. Experimentally and clinically it has been shown that the estrogenic hormone stimulates growth of the uterus and the luteal hormone has been shown to have an antispasmodic effect on the uterine muscles.

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In many cases of severe menstrual pain there is an abnormal nervous background and the tolerance to pain is lowered. These undoubtedly are etiologic factors and careful attention to the psychic and physical habits of the afflicted young women often is more effective in obtaining relief than is the use of drugs.

A review of the literature fails to reveal an analysis of a series of cases of dysmenorrhea in which treatment has been by various methods and the patients have been observed for a sufficient length of time to establish definite conclusions regarding the efficiency of the various methods of treatment available. Boynton has outlined a controlled study of cases of dysmenorrhea but sufficient time has not elapsed to allow the ultimate results of treatment to be reported.

The report of the following study is of questionable value because of (1) the difficulty in evaluating the answers to the questionnaires sent these patients, (2) the irregularity with which the patients took the medicine prescribed and (3) the fact that severity of the pain in some cases required administration of an analgesic while the more slowly acting medicine was being tried out. While nothing new is offered regarding the etiology or the cure of dysmenorrhea we felt that study of the cases would be of interest and perhaps of some value.

THE INVESTIGATION

From Jan. 1, 1931, to Jan. 1, 1934, 682 cases in which a diagnosis of dysmenorrhea was made were encountered at the Mayo Clinic. Of these, certain cases were excluded from the study: (1) In 112 cases dysmenorrhea was incidental to the chief complaint or was not of sufficient importance to require medication. (2) In 37, surgical operation was advised but the patients refused to submit to it. (3) In 104 cases some surgical procedure was carried out; dilatation and curettage, suspension of the uterus, resection of presacral nerves, and hysterectomy constituted the majority of these operations. (4) In 38 of the cases some pelvic pathologic condition was deemed responsible for the pain. Because this study was undertaken to determine the efficacy of the various drugs and hormones, only cases in which pelvic examinations revealed normal reproductive organs were reviewed. (5) Replies to follow-up letters were not received from 129 of the patients treated medically. This study, therefore, is based on a review of 262 cases.

Some incidental observations made in the survey may be of interest. There were 132 single patients; of the 130 married women 47 had had children when the study began. Thus of the married women 36.1 per cent had not been benefited by that age-old "cure" of dysmenorrhea, the bearing of children. However, 22 patients subsequently became pregnant and of these, six were completely relieved, the dysmenorrhea returning after varying intervals of time, and the dysmenorrhea of six was not affected in any way by pregnancy.

In the histories of 82 of the 262 cases were noted psychic factors such as "chronic nervous exhaustion" or "nervous instability," which often are responsible for lowering the threshold for pain of the individual. Headache and migraine were associated with the pelvic pain at menstruation in 43 cases. Forty-three patients had already submitted to pelvic operation in an attempt to obtain relief but without the desired result, but the normal condition of the reproductive organs was not affected.

For convenience in evaluating treatment the following classification was made according to the treatment given: (1) antispasmodics; benzyl benzoate, belladonna, calcium, viburnum; (2) analgesics, such as a preparation of amidopyrine plus a derivative of barbital known as cibalgin; (3) sedatives, such as phenobarbital (elixir of luminal) and the bromides; (4) endocrine products: estrin (progynon), luteolipoid of corpus luteum (sistomensin), ovarian extract, placental hormone (emmenin); (5) roentgen therapy: (a) light dosage to ovaries and pituitary, or (b) menopausal dosage over the ovaries; (6) radium. Frequently treatment belonging in more than one group was prescribed in a single case, and in these cases we have attempted to credit each preparation as best we could from the replies received from the patients. The results have been gathered and presented in Tables I, II, and III to facilitate comparison. "Complete relief" indicates either entire disappearance of pain at the periods of flow or control of the pain while using the treatment; similarly, "partial" or "improved" refers to permanent lessened severity of the pain or lessened severity of the pain during treatment.

One hundred and thirty-nine patients received, as the main medication, one or more of the analgesics, antispasmodics or sedatives (Table I). Of these, 71, or 51 per cent, received benefit. Three of these reported that they rarely had any discomfort subsequent to a course of medication. In these 3 cases cibalgin (two years), cibalgin and belladonna (one and a half years with an occasional dose thereafter), and calcium lactate (the patient was still taking it at the time of writing) were used.

Some one of the endocrine preparations, either alone or together with analgesics, was prescribed in 129 instances (Table II) and 78 of the patients (60 per cent) were relieved of the dysmenorrhea. Of the patients who received the endocrine preparations a large percentage gave histories of an irregular cycle, of menorrhagia, or of oligomenorrhea as well as of dysmenorrhea, and an attempt was made to select the preparation which at that time was considered indicated in the individual case to control the menstrual irregularity as well as the dysmenorrhea.

In the 36 cases in which ovarian extract was given, all types of variation of the menstrual cycle were noted. Of the 4 patients who reported complete relief of the dysmenorrhea while the medication was being given, 1 was still using the treatment when this study was made; 2 reported little or no pain without the medication, and 1, after having secured complete relief for three months from ovarian extract alone, and for one year from anterior pituitary and ovarian extract combined (given elsewhere) was troubled with a gradual return of the severe dysmenorrhea at the time of writing this report. Of the 17 patients whose condition was improved by the use of ovarian extract for varying periods of time, 12 reported that they subsequently had dysmenorrhea such as had troubled them before treatment and 5 had pain which was not as severe as that experienced before treatment.

Of the 22 patients who received progynon, the menstrual cycles of only 5 were irregular. The periods of 2 of the 5 became regular, and of 2 the cycles remained irregular after medication. One of the 6 patients who obtained no relief from medication has since had a baby, with temporary relief of menstrual pain but with later return of severe pain. The condition of another was improved for some months after the medication. Later she had a miscarriage, with relief of the dysmenorrhea for a short while; although the dysmenorrhea had returned it was not as severe as it had been formerly. The 15 patients who received benefit from the treatment in lessened severity of dysmenorrhea (Table II) are of particular interest. Improvement of two of these remained permanent after discontinuation of the medication. The dysmenorrhea of 13 of the patients who were relieved while taking progynon became severe again after medication had been stopped for several months. One patient reported that the next period after discontinuation of the treatment was ac-

TABLE I. SUMMARY OF RESULTS OF TREATMENT CHIEFLY* WITH ANALGESICS, ANTISPASMODICS, AND SEDATIVES

SUBSTANCES ADMINISTERED		TOTAL CASES	RELIEF OBTAINED, CASES		
SUBSTANCE OF MOST IMPORTANCE	COMBINED WITH		COMPLETE	IMPROVEMENT ONLY	NONE
Benzyl benzoate (benzylolates)	Nothing else	18	0	9	9
	Amidopyrine + derivative of barbital (eibalgin)	6	0	2	4
	Endocrine products	10	0	3	7
Amidopyrine + derivative of barbital (eibalgin)	Nothing else	18	1	9	8
	Belladonna	16	1	7	8
	Hammond's mixture	4	0	1	3
	Calcium lactate	5	0	4	1
	Acetylsalicylic acid (empirin)	1	0	1	0
	Endocrine products	25	4	15	6
Belladonna	Nothing else	2	0	0	2
	Phenobarbital (elixir of luminal)	9	1	3	5
	Hammond's mixture	1	0	1	0
Hammond's mixture	Nothing else	5	0	2	3
Viburnum	Nothing else	7	0	4	3
Acetylsalicylic acid (empirin)	Nothing else	1	0	1	0
Phenobarbital (elixir of luminal)	Nothing else	3	0	0	3
Calcium lactate	Nothing else	3	1	0	2
	Luteolipoid of corpus luteum (sistoneusin)	5	0	1	4
Totals		139	8 (5.7 per cent)	63 (45.3 per cent)	68 (48.9 per cent)

*The endocrine products represented in the table apparently had little, if any, effect.

TABLE II. SUMMARY OF RESULTS OF TREATMENT CHIEFLY WITH ENDOCRINE PRODUCTS

SUBSTANCES ADMINISTERED		TOTAL CASES	RELIEF WHILE TREATMENT WAS CON- TINUED, CASES			RETURN OF PAIN ON CESSATION OF TREATMENT, CASES		
SUBSTANCE OF MOST IMPORTANCE	COMBINED WITH		COMPLETE	IMPROVEMENT ONLY	NONE	MILD	SEVERE	
Ovarian extract	Nothing else Analgesics	16 20	4	17	15	5	12	
Estrin (progynon)	Nothing else Analgesics	16 6	1	15	6	0	13	
Luteolipoid of corpus luteum (sistomensin)	Nothing else Analgesics	8 19	1	15	11	0	15	
Placental hormone (emmenin)	Nothing else Analgesics	18 26	1 0	10 14	7 12	8	13	
Totals		129	7 (5.4 per cent)	71 (55 per cent)	51 (39.5 per cent)	13 (10 per cent)	53 (41 per cent)	

accompanied by the usual pain. Five of the 13 women were able to remain comfortable with the aid of analgesics of the type of acetylsalicylic acid after they discontinued the use of progynon. One has since been relieved entirely by insertion of a silver spring pessary by her home physician. Two of the patients whose condition was improved had undergone previous operations for dysmenorrhea without benefit.

Of the 27 patients who received sistomensin, 9, or 33 per cent, had menorrhagia and in those cases sistomensin was chosen because of a desire to lessen the amount of bleeding as well as to observe the effect of the preparation on the dysmenorrhea. Five of these patients have reported a normal amount of flow. The menstrual cycle of all but four patients of this group was regular. The pain of one patient was completely relieved for one year. Later she reported, however, that she had severe pain until the flow began. Fifteen obtained partial relief which lasted from a few months to three years following treatment; all have reported return of the severe pain after discontinuing the medication. One of them has been entirely cured by dilatation and curettage performed later elsewhere.

Of the 44 patients who were given emmenin, 11 (24 per cent) had irregular periods and the cycles of 4 of these 11 patients subsequently became regular. One woman, twenty-two years of age, who had had dysmenorrhea for two years, was completely relieved of pain after she had taken emmenin for only one month. Eight of the patients whose dysmenorrhea returned after cessation of the medication have reported that the pain is less severe than it was before treatment. Thirteen who had been relieved while taking emmenin said that the dysmenorrhea was as severe after discontinuing the medication as it had been before the start of medication.

TABLE III. SUMMARY OF RESULTS OF TREATMENT WITH ROENTGEN RAYS AND RADIUM

KIND OF TREATMENT	DOSE	TOTAL CASES	RELIEF ATTRIBUTABLE TO TREATMENT, CASES		
			COMPLETE	IMPROVEMENT ONLY	NONE
Roentgen rays	Light	2	2	0	0
	Menopausal	3	3	0	0
Radium	360 to 780 mg. hr.	6	4	1	1
	Menopausal	5	2	0	3
Totals		16	11 (69 per cent)	1 (6 per cent)	4 (25 per cent)

Two of the 5 patients (Table III) who received roentgenologic treatment were given a light dose of roentgen rays, the so-called stimulating dose. This light dose was given over the pituitary gland in one case and over the ovaries in the other, with relief of pain for six months in both cases, at which time the treatment was repeated, again with relief. Because of the danger of too heavy exposure, this method of treatment should be used very cautiously and only by roentgenologists of experience. Three patients aged twenty-six, thirty-seven, and forty-three years, respectively, had a satisfactory menopause following a menopausal dose of roentgen rays.

A number of years ago one of us (L. J. S.) observed that temporary cessation of menstruation subsequent to the uterine application of a small amount of radium was followed by reestablishment of the menstrual cycle without pain although previously menstruation had been accompanied by severe pain. As a result of this observation, 11 patients of this series (Table III) were given intrauterine radium treatment, 6 receiving a small dose. Of these, 3 received 360 mg. hr. and 3, 400,

450, and 780 mg. hr., respectively. These patients were carefully selected and were given the radium only after other means had failed to give relief. One patient, aged thirty-five years, who received 450 mg. hr., ceased to menstruate after three and a half years of painless regular periods. Normal menstrual periods were resumed without pain in three other instances. Irregular menstruation, but accompanied by very little pain, occurred in one case and in one instance the patient continued to have dysmenorrhea. The 5 patients who were given what was considered a menopausal dose of radium were aged thirty-two, thirty-six, forty-two, forty-two, and forty-six years, respectively, and received an average of 1,100 mg. hr. of intra-uterine radium treatment. In only 2 cases did menstruation cease; in another, after eight months of amenorrhea, painful but regular menstruation returned. In one case, after six months of amenorrhea, painful irregular flow returned, continued for several years and then permanent amenorrhea appeared. This patient was forty-seven years of age when this report was written. The fifth patient reported that she was having very irregular and painful menstruation. The choice of the menopausal dose of radium was dictated in these 5 cases by several factors: the greater age of the patients, the presence of menorrhagia and the failure to control the dysmenorrhea by less radical measures.

For those patients who are incapacitated for one or more days every month and who have not benefited by medical and hygienic measures conscientiously followed for several months, resection of presacral nerves is to be considered. The results obtained at the Mayo Clinic by this procedure are not included in this study but have been reported by Counseller and Craig and by Adson and Masson, who obtained 100 per cent relief of pain in 9 cases, 95 per cent relief in 2 cases, and 75 per cent relief in 3 cases following the operation. Careful selection of patients should be made for this operation, especially with regard to the nervous stability. The nervous, high-strung girl is very likely to become more nervous and introspective and the family more concerned about the girl's invalidism following any surgical procedure.

COMMENT

Primary ovarian functional dysmenorrhea is an economic and social handicap for a considerable number of women and a review of the results of attempts to remove the cause of the pain is indeed cause for discouragement.

Nervous instability and lowered tolerance of pain may be contributing etiologic factors when the patient is a slender, studious girl who has esthetic tendencies and who shuns physical activity, but dysmenorrhea afflicts also the vigorous, athletic girl of excellent nervous stability. Much can be done to relieve the moderate dysmenorrhea by intelligent attention to psychic factors and by improving the general physical condition by systematic physical exercises and by control of constipation. More definite knowledge of the function of the various endocrine glands and of the rôle played by the hormones may throw light on the etiology of dysmenorrhea and thus offer means of controlling the pain.

Review of the cases which form the basis of this study discloses that the antispasmodics, such as benzyl benzoate, gave relief in 50 per cent of the cases. In about 50 per cent of those cases in which dysmenorrhea was associated with irregularity of the menstrual cycle the use of the estrogenic substances, emmenin, progynon and sistomensin, controlled the pain. For those patients in treatment of whom the more simple medical measures are ineffective, more radical measures must be considered rather than resorting to the use of opiates. Resection of the presacral nerves or small doses of radium or roentgen rays are to be carefully considered as means of obtaining relief for the patient when other methods have failed.

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CLINICAL OBSERVATIONS ON THE EFFECT OF 800 K.V. ROENTGEN RAYS IN UTERINE CARCINOMAS*

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FROM May 15, 1933, to June 1, 1934, eighty-nine patients with carcinomas of the female generative organs were admitted to the Mercy Hospital Institute of Radiation Therapy. Seventy-eight carcinomas were treated with 800 K.V. roentgen rays. The time elapsed in these cases since the termination of the treatment, therefore, has been from twenty-four to thirty-six months. It is too early to report permanent or absolute cure rates, which must be based on a survival rate of the conventional five years. However, a survey of the clinical results at this time may enable one to form a relative opinion on the therapeutic efficacy of 800 K.V. roentgen rays in comparison with that of 200 K.V. roentgen rays which are at present almost universally employed in the so-called combined method of radiation treatment with radium and roentgen ray in uterine carcinomas.

The objects of this report are twofold, namely to present the early local effects and the constitutional reactions produced with the therapeutic use of 800 K.V. roentgen rays. A discussion of the technical and physical details has been omitted. Those interested in these phases of radiation therapy are referred to the literature.¹

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THE LOCAL RESULTS OF TREATMENT

The early local effects of radiation therapy coincide with the survival rates attained at the end of thirty-six months, which are tabulated in Table I. The carcinomas are divided into primary and recurrent. These main divisions are again subdivided into four clinical groups, namely:

- Clinical Group I: The *clearly localized* carcinoma;
 Clinical Group II: The *doubtfully localized* carcinoma;
 Clinical Group III: The *invading growth*; and
 Clinical Group IV: The *terminal or fixed growth*.

The clearly localized growth should not be larger than 1 cm. in diameter, and the uterus should be normally movable. The doubtfully localized growth may involve almost one-half of the vaginal portion of the cervix, but it apparently is still limited to the uterus, which, however, is not normally movable due to loss of elasticity of the paracervical tissue from inflammatory or neoplastic changes. The invading growth is characterized by an invasion with cancer of the parametria, constituting the suspension apparatus of the generative organs. The tumor mass as such is movable, but movability is restricted. The terminal carcinoma means a fixed tumor due to a frozen pelvis, or an invasion of the vaginal walls, the urinary bladder, or the rectum, or the formation of distant metastases.

The results of treatment are designated as arrested or not improved. If symptomatic or anatomic healing ensued, determined by follow-up examinations at monthly intervals, then the tumor was considered arrested in growth. If the patient succumbed, or the tumor remained active, or the patient did not report for follow-up, then the tumor was not improved.

TABLE I. RESULT OF TREATMENT

CLINICAL GROUP	NUMBER	ARRESTED	NOT IMPROVED	NUMBER	ARRESTED	NOT IMPROVED
I	1	1				
II	5	4	1			
III	14	9	5	8	3	5
IV	10	3	7	40	8	32
Total	30	17	13	48	11	37

There were three stump cancers in the primary and five stump cancers in the recurrent carcinomas, that is 10 per cent. The percentage of arrested primary cancers is 56.67 and of arrested recurrent cancers 22.92.

These values without any other qualification would be of only minor importance. However, their significance is enhanced compared with similar percentages of local results obtained in the radiation treatment of cancers subjected to different technics, that is with radiations of different qualities or lower voltages. Four periods have been studied in

the clinic. The factors of the technic of each period are shown in Table II. The cases admitted during one year of each period were taken and then divided according to the results of treatment at the end of eighteen months (see Table III).

TABLE II

PERIODS	RADIUM MG. EL. HR.	ROENTGEN K.V. MAX.	F. S. D. CM.	FILTER IN MM.			FIELDS		H. V. L. IN MM. CU.	R. IN AIR
				AL.	CU.	SN.	SIZE AND NO.			
1914 to 1921	3600	90 to 140	30 to 65	10.0 or 1.0			25 or 225	9 to 14 or 2 to 4	0.5	675
1921 to 1925	3600	200	65	1.0	1.0		300	2 to 4	1.58	900
1926 to 1932	3600 to 4800†	200	65	1.0 1.0	1.0 2.0		300	2 to 4		1375*
1933	1200	800	70	3.0	4.5	1.56	300	2 to 4	8.80	3000†

*Five fraction doses each of 275 r. every other day to each field.

†Ten fraction doses one every other day to each field.

‡Three fraction doses each 1,500 to 1,600 mg. el. hr. in eight-day intervals.

TABLE III. RESULTS OF TREATMENT AT THE END OF EIGHTEEN MONTHS

PRIMARY				RECURRENT		
YEAR	NUMBER	ARRESTED	NOT IMPROVED	NUMBER	ARRESTED	NOT IMPROVED
1914	22	5	17	10	0	10
1921	37	11	26	9	2	7
1926	19	7	12	2	1	1
1933	30	17	13	48	11	37

The percentages of survivals after eighteen months in the primary cases were 22.7 per cent in 1914; 37.8 per cent in 1921; 36.84 per cent in 1926; and 56.67 per cent in 1933. The absolute curability percentages in these periods were 14.70 in 1914; 26.77 in 1921; and 30.92 in 1926. Hence the ratio between the preliminary results at the end of eighteen months and the absolute curability rate is as follows:

TABLE IV. RATIOS BETWEEN THE PRELIMINARY AND FIVE-YEAR CURE RATES

PERIOD	PRELIMINARY RATE AT 18 MONTHS	ABSOLUTE CURABILITY	RATIO
1914	22.7	14.7	3 : 2
1922	37.8	26.77	4 : 3
1926	36.84	30.92	6 : 5
1933	56.67	?	?

These ratios may be applied to the preliminary results obtained with 800 K.V. roentgen rays. It has been our observation that the five-year cure rate increased invariably with an improvement in the quality of roentgen rays, as the radium dose remained practically the same. The difference in treatment between the periods of 1922 to 1925 and 1926

to 1933 has been in the time spacing; during the period 1922 to 1925 the entire treatment was completed within seven days and during the period 1926 to 1933 within twenty-one to twenty-eight days. The time spacing permitted an increase in the total radiation dose used in the 1922 period of about 35 per cent. The five-year cure rate was increased 4 per cent.

Should the ratios seen in Table IV prevail then the 56.67 per cent would be reduced to about 35 per cent if the first period ratio prevailed; to about 40 per cent if the second-period ratio proved effectual; and to about 45 per cent if the third-period ratio were applied. I do not wish to make predictions or to be speculative. The results attained under similar conditions in the previous periods justify the statement that the five-year curability rate should improve as the preliminary subjective and objective results have improved formerly with an increase in the voltage or a decrease in the wave length of the roentgen rays.

The results of treatment in the recurrent carcinomas are negligible from a curative viewpoint; but noteworthy from a palliative standpoint. Results should become improved if the surgeon would refuse to operate without preoperative, adequate radiation treatment or would refer the patient for adequate radiation treatment immediately after operation. A perusal of the allotment of the recurrent carcinomas to the clinical groups reveals that patients came late usually during the terminal stage. A recurrent carcinoma should not be treated until the clinical diagnosis has been corroborated by a histologic diagnosis. This is especially important in carcinomas recurrent after radiation treatment. The ulceration may be carcinomatous or inflammatory due to radiation necrosis. A repetition of the radiation treatment when radiation necrosis is present would then be directly disastrous.

The palliative results obtainable with 800 K.V. roentgen treatment are at times remarkable. Palliation is especially seen in carcinomas causing pelvic pain due to invasion of or pressure on the pelvic sensory nerves or to edema of the legs from lymph stasis by pressure of the fixed carcinomatous infiltrations on the blood and lymph vessels or obstruction of the ureters by invasion or by compression. Such palliation is mostly seen after the application of about 50 per cent of a tolerance skin dose to the midpelvis. This dose measures about 1,500 to 1,800 r. without backscatter in the midpelvis. Pelvibimanual examination reveals then a softening of the indurated tissues or a return of mobility of the tumorous masses. If objective or subjective improvement is not attained after the application of one-half of the total dose, then the outlook for an arrest of the primary cancer or a relief from parametrial invasion or compression of nerves, blood vessels, or ureters is probably very poor.

The sequence of the local reactions was as follows: Palliation of pain and total arrest of bleeding occur with the onset of reduction in the size of the tumor and appear about the midperiod of the treatment.

Absorption of the growth would be completed within two to six months. The rate of resolution depends on the size of the growth, on the amount of connective tissue cells in the growth, and the character of the tumor cells as radiation sensitivity, cell type, modification of the cells caused by previous radiations.

The local changes in the skin consist of epilation and erythema after a dose of about 50 per cent of the total dose, and exfoliation with a wet dermatitis at the termination of the treatment when the full dose has been given. The mucosae of the vagina, urinary bladder, and rectum assume a deep red color after about 50 per cent of the total dose has been applied and a white pseudodiphtheritic mucositis at the end of the treatment. The deep red discoloration reaction is accompanied by frequent and painful urination and diarrhea. The skin and mucosa reactions subside within four to six weeks. The tanning of the skin is negligible, and the hair regrows invariably.

GENERAL CONSTITUTIONAL REACTIONS

So-called radiation sickness as nausea and vomiting is hardly ever seen, though anorexia may become troublesome in the latter half of the course. It probably results from an alkalosis. The pH determinations of the blood are being undertaken, but a conclusion has not as yet been reached.

Gain in weight and strength may occur during the course of treatment coincident with the cessation of bleeding, ulceration, infection, and toxemia. It, however, may run a slow course after the treatment, coinciding more nearly with the gradual response of the tumor to radiation. Gain in weight and strength is a favorable prognostic omen; loss of the same is usually a sign of the continuance of the destructive ravages of the cancer.

Blood examinations² have been made routinely and at stated intervals. The erythrocyte count, hemoglobin percentage, leucocyte and differential count have been determined before the beginning of treatment and after the fifth, tenth, twelfth, fourteenth, eighteenth, and twentieth treatments in 60 consecutive cases. Significant decreases in the erythrocyte count (300,000 or more) occurred in only 10 cases, and were practically always associated with far-advanced malignant disease. In six instances there was a definite increase in the number of erythrocytes during the course of treatment. The remaining cases showed no significant changes.

Changes in the erythrocyte count were usually but not always accompanied by a corresponding change in the percentage of hemoglobin. In three cases, the hemoglobin percentage fell 10 to 15 points without any decrease in the erythrocyte count.

Changes in the leucocyte count occurred more frequently and were more pronounced than the changes in the erythrocyte count or hemo-

globin. The leucocyte count dropped to or below 4,000 in 21 cases. In 19 of these cases, the leucopenia was very transient and the differential counts remained normal. Only two instances of stubborn leucopenia were observed and these were both associated with multiple metastases to the bones.

These observations may be summarized as follows:

1. There is early relief from subjective symptoms such as pain, distress, discharge and bleeding, which is evident at about the midperiod of the treatment, that is from the fifteenth day on, as the course is extended over four weeks. The relief is permanent with an arrest of growth, and the symptoms reappear with a recurrence.

2. The systemic reactions are mild. Nausea, vomiting, and loss of appetite are infrequent. This is very apparent to one familiar with medium voltage therapy, i.e., 180 to 220 K.V. maximum. At the onset of the skin reaction and mucositis, symptoms referable to these complications arise, as burning and itching of the skin, frequent and burning urinations, and frequent watery and mucous stools. They appear about the twenty-first day, reach a climax at about the fifth or sixth week, and then gradually abate until complete healing has occurred at about the seventh to eighth week.

3. The effect on the growth is seen early. If no decided reduction in size of growth occurs at about the twenty-first day, then it may be assumed that total arrest or resolution of the growth will usually not occur.

4. The effects on the normal tissues of the skin and mucous membranes are erythema, epilation, exfoliation and secretion in the former, and erythema, pseudodiphtheritic mucositis, and watery and mucous discharge in the latter. They disappear at about the sixth to seventh week. The hair regrows almost invariably, the tanning is slight, and healing is seen by the end of four to eight weeks. Induration of the skin is not seen. If the general health of the patient had not been unduly lowered, as seen in advanced and infected cancers, the effect on the blood count did not show any marked reduction in the number of red and white cells or the percentage of hemoglobin.

5. The early results of treatment at an interval of twenty-four to thirty-six months after completion of the radiation treatment are very encouraging. Should these results become modified at the end of five years in the ratios seen with technics employing 140 to 200 K.V. roentgen rays, then a marked increase in the five-year curability rate should be attained.

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ON THE OBSTETRIC MANAGEMENT OF PREMATUREITY

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MEDICAL literature contains many studies of premature infants but, until the recent reports by Clifford from the Boston Lying-In Hospital,^{2, 3} nearly everyone has considered the premature as essentially a pediatric problem. Capper¹ observed that the early and correct application of forceps did not increase the danger of intracranial hemorrhage. A few others compared the mortality with the cause of prematurity, but the Boston studies were the first to show the marked bearing of the type of delivery upon the mortality.

It has been the opinion of our department for some time that delayed delivery would markedly decrease the premature's chances for life. Therefore, in studying our records of prematurity at the Western Pennsylvania Hospital, particular attention has been paid to the type of delivery and its relation to the infant's survival. That this report confirms our opinion is incidental. The essential fact remains that entirely too great an emphasis has been placed upon the problems of feeding and nursery care, at the expense of an almost utter neglect of the most important problem, the conduct of labor.

During the period from June 1, 1924, to March 1, 1935, there were 10,396 deliveries in this hospital with 349 living premature infants, for an incidence of 1:29.7 deliveries. These infants suffered a gross mortality of 53.2 per cent, with 36.4 per cent during the first twenty-four hours and 41.8 per cent within the first forty-eight hours. With such a preponderance of the deaths occurring in the first two days, it behooves us to inquire into the causes of them, both immediate and remote.

Feeding and kindred nursing problems were handled in essentially the same manner during the entire period. We have felt that the use of an incubator or thermostatically controlled nursery does not justify itself, and so each baby is kept in a separate premature bed. Each bed has a compartment for the baby 18 inches deep, 42 inches long, and 32 inches wide. It is covered at the ends and sides by a double quilted pad containing pockets for hot water bottles. There is a rubber covered mattress on the bottom. A bath thermometer stays beside the baby so the nurse can keep the temperature at 90° F. by regulating the hot water bottles. Our experience has been that by placing the responsibility of controlling the temperature of the bed directly with the nurse, there has been a minimum of temperature variation. She knows that everything depends upon her, and is never lulled to a false sense of

security by an impressive maze of thermostatic controls. Before a premature baby is born, one of these beds is prepared in the nursery and taken to the delivery room so that the baby is never chilled.

It should not be necessary to emphasize the value of breast milk to infants in general, and above all to prematures. Suffice it to say that, whenever possible, these babies were fed wholly upon breast milk. Lacking mother's milk, the entire feeding, or the necessary balance, was a modified cow's milk formula. Feedings were begun when the baby was six hours old and repeated at two-hour intervals until sufficient was taken to allow the infant to change to a three-hour schedule and continue to gain weight. Depending upon the strength of the individual infant, it was fed either by gavage, Breck feeder, bottle, or direct nursing at the breast.

The only addition to the above general outline is that for the past four years we have been administering fresh citrated blood to small or delicate babies. Our purpose is to reduce the tendency to hemorrhage and to supply an easily assimilable food, where a baby is not eating well or is markedly jaundiced. The blood is taken from either parent, or from another healthy donor, without typing. It is given within an hour or two following the delivery and repeated in from twenty-four to seventy-two hours, if the condition of the baby indicates it and the previous injection has been absorbed. The blood is given in the back, intramuscularly, from 15 to 50 c.c. in amount. Unfortunately we have no adequate data on this particular procedure; yet while no definite conclusion can be drawn, we are of the opinion that it is a very definite benefit.

Since these babies are placed in heated beds at birth, they are never chilled. All feeding is done by expert graduate nurses. Of course, the very immature infants, incapable of a separate existence, will succumb very quickly. But can we blame nursery care and immaturity entirely for the heavy mortality seen in the first forty-eight hours? Possibly, but not without looking for and ruling out all other factors beforehand.

What other factors should we consider? Let us examine the sex, the birth weight, the cause of prematurity, the cause of death, and last, the type of delivery.

Sex seems to have only a slight influence, with the mortality among the males being 54.1 per cent while that of the females was 51.4 per cent. This difference of less than 3 per cent does not indicate a great deal, and so we feel that sex is, at best, a negligible factor in this study.

On the other hand, the weight has a very marked bearing upon the mortality and would seem to be our best prognostic criterion. From Fig. 1 we learn that as the birth weight increases, there is a steady almost proportionate decrease in the death rate. Hence, other factors being equal, the larger the premature baby at birth, the better its chance of survival.

In studying the cause of prematurity and its bearing upon the mortality, we can consider only those cases with definite or apparent findings. In this series there were 191 of such, divided among four major groups.

The largest group of known cause (21.7 per cent) was that attributed to a multiple pregnancy. Of 75 babies in this group, 22 (29.3 per cent) died, giving to the group the lowest mortality. Toxemia of pregnancy resulted in 24 babies or 9.7 per cent of the total, with a mortality of 41.7 per cent. This small group can be subdivided into 11 who went into spontaneous labor with a mortality of 36.4 per cent, and 21 in whom labor was induced by artificial rupture of the membrane with an infant death rate of 42.9 per cent. There were 59 cases where the only apparent cause of premature labor was a spontaneous rupture of the membrane and of them we lost 46.4 per cent. Of 25 babies whose prematurity was attributed to maternal bleeding the mortality was 34.8 per cent. They were subdivided with 6 spontaneous labors and a loss of 75 per cent and 19 whose labor was induced with a mortality of 33.8 per cent.

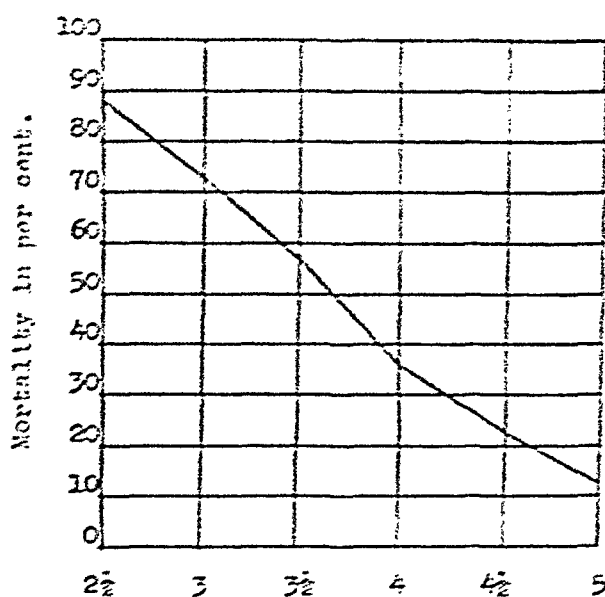


Fig. 1.—Birth weight in pounds.

In this series, multiple pregnancy gives the lowest mortality while the spontaneous group comes next. The maternal toxemia group is small and the difference in results between spontaneous and induced labor is very slight. Therefore, in spite of our figures to the contrary, we feel that where the mother's toxemia is not quickly controlled, and the baby is apparently viable, its chances of survival are enhanced if labor is induced by simple rupture of the membranes. Maternal bleeding, for obvious reasons, yields the highest infant mortality. Even though born alive, such babies have suffered more or less intrauterine asphyxia so that, even without the extra birth trauma, they are extremely likely to develop cerebral hemorrhage. This brings us to a consideration of the cause or causes of death among premature infants.

With nearly four-fifths of our total mortality occurring within forty-eight hours of delivery, it would seem that feeding and nursery care

are, at best, of secondary importance. Not that we wish to minimize the value of either, for both are decidedly essential. Rather, we must admit that most of the deaths occur before either of these factors has had time to be of any material influence. Unfortunately our records are based, to a large extent, upon the clinical diagnosis with very few autopsies to give pathologic support. According to these records, cerebral hemorrhage accounted for only 9 (4.7 per cent) of the 186 deaths. Atelectasis caused an equal number, while asphyxia is credited with 6 (3.2 per cent). By far the greatest number, 145 or 77.9 per cent of the total, was attributed only to prematurity. In contradistinction to this, Hess⁴ has reported on 307 premature deaths of which 246 were autopsied. Of these latter, 107 or 43 per cent were definitely proved to have an intracranial hemorrhage. On the basis of this report, it would appear that our incidence of 4.7 per cent is far too low, and that intracranial hemorrhage should be considered as the major cause of death in premature infants. This being the case, we should find that the lowest mortality would be found following the least traumatizing labor and that the converse would also be true.

Therefore, let us consider the types of delivery and see if any significant facts may be learned. Of 52 forceps deliveries, 17 or 32.6 per cent died, yielding the lowest mortality for any type of delivery. As a contrast, we find 203 spontaneous live births with a loss of 113 or 55.6 per cent and, while this is second only to the forceps cases, it is already higher than the total gross percentage. In third place we have the group of 23 versions with a loss of 13 or 56.5 per cent, while in 51 breeches there was a mortality of 35 or 57.3 per cent. These percentages are very slightly higher than those shown in spontaneous deliveries and, we feel, should argue convincingly for reducing the time of labor. If the length of labor were the only factor, then cesarean section should show us the best record of all but, strange to say, this is not the case. In our series of ten sections we lost 80 per cent of the babies. This being even higher than that reported by Clifford,² we heartily agree with his conclusion that, "The present technic of cesarean section is one of the most hazardous methods that can be used for the delivery of premature infants." He suggests that this might be due to the preoperative use of morphine. Since we never use this drug prior to delivery of the baby in cases of cesarean section, we must look elsewhere, for morphine certainly cannot be the cause of our high mortality.

Can we attribute the mortality to the same cause which was our indication for cesarean section? Let us review these cases to see if there is anything to serve as an explanation. Three cases were repeat sections done because labor began prematurely, and all the babies were lost, as was one in the case of an elective section for a generally contracted pelvis. Two cases of mitral valvular disease were sectioned. The first baby died of cerebral hemorrhage. The second patient had twins, one

of which died in two days, while the second died on the ninety-eighth day of malnutrition. In two cases of placenta previa, one baby died in five hours, while the second survived, and in one case of cervical carcinoma the baby also survived. Three babies weighed over four pounds and two of them survived. Thus it would seem that a baby under four pounds has only a slight chance of survival. One indication for the operation is about the same as another and the small babies can rarely survive. Since there is no birth trauma, and since we do not use morphine preoperatively, the one common factor remaining would seem to be the inhalation anesthetic given the mother. The anesthesia is more prolonged for a section than for a forceps delivery. This may account for the heavy mortality or it may not, but it might be worthwhile to try a few such cases with spinal or local anesthesia, by way of comparison.

SUMMARY

1. With over four-fifths of our total premature mortality occurring within forty-eight hours of delivery, we must look to other factors than feeding and nursery care to account for it.

2. As the birth weight increases, so do the chances for the infant's survival.

3. Multiple pregnancy and maternal toxemia give us the best results among the known causes of premature labor, while antepartum bleeding acts as the greatest cause of infant death.

4. Forceps delivery offers the best method for handling premature labor and cesarean section, as now done, the worst.

CONCLUSION

The subject of prematurity warrants further study from the obstetric viewpoint. The method of delivery is a tremendous factor in the ultimate outcome of these infants.

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902 PEOPLES EAST END BUILDING

Ozaki, M.: A Histologic Study of the Peripheral Nerves in the Human Female Genitalia, Jap. J. Obst. & Gynec. 19: 2, 1936.

In an extensive investigation of the nerve distribution of the uterus, contrary to general opinion, Ozaki found nerve elements in fibromyomata of the uterus.

J. P. GREENHILL.

POSTOPERATIVE URINARY TRACT SEQUELAE IN TOTAL HYSTERECTOMY

A CYSTOSCOPIC STUDY OF 200 CASES

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IT IS the generally accepted belief among surgeons that trauma to the bladder and ureter is a common and serious complication in total extirpation of the uterus. Bland lists five types of total hysterectomy as the five most frequent causes of ureteral injury. Many articles have appeared to substantiate this claim. All have been based on proved cases appearing in a series of hysterectomies, and their conclusions are incontestable.

Injury is not always recognized at the time of operation. A fatal peritonitis may result from an unnoticed rent in the bladder with the escape of urine. Complete anuria or the presence of hematuria may reveal ligation or other injury to the ureter. The appearance of vesical or ureteral fistula may be the first notice of operative injury. Still later manifestations may be hydronephrosis, pyonephrosis, or complete atrophy of the kidney, often with no warning symptoms for months after operation. Bladders of small capacity may result from the attachment of the vesical peritoneum to the reconstructed pelvic sling made by suturing together the broad ligaments after hysterectomy. These patients complain of urinary frequency and urgency and are often believed to have cystitis or trigonitis.

Much has been said about ureteral injuries discovered after operation. It is generally believed that many are never recognized.

Harris reports a case in which serious symptoms did not occur until nine years after the operation. Newell states that there are no definite symptoms in unilateral ligation of the ureter and that death of the kidney occurs before the ligature is absorbed. Bland, in a comprehensive review of the literature, collected 316 cases of surgical injury of the ureter. Personal communications from 51 other surgeons yielded an additional 125 cases. Bland says, "Despite prevailing belief that ureteral damage is rare, I believe it to be one of the most, if not the most frequent, as well as the most serious accidents of pelvic work. . . . No doubt a certain number of ligations occur which are never recognized and which do not provoke symptoms though kidney destruction is inevitable." Morris and Brunton, speaking of traumatism to the ureter, say, "The effects may not be observed immediately and in the majority of cases they are not. The patient may go for months or perhaps years without any operative lesion being discovered."

Our attention was drawn to this problem by a patient, Florence E., forty-seven years old, colored, who was operated upon July 11, 1934,

by one of us. A perineorrhaphy, abdominal panhysterectomy, bilateral salpingo-oophorectomy, and appendectomy were done. The postoperative course was entirely uneventful. Maximum temperature was 38.5° C. There were no urinary symptoms. The patient was discharged on the twelfth postoperative day in good condition. Four weeks after operation a watery vaginal discharge was noted. Investigation revealed a ureteral stricture and a ureterovaginal fistula on the right side 4 cm. above the ureterovesical orifice.

This case suggested to us that such injuries with an asymptomatic latent period might indeed be more frequent than we realized. We were unable to find in the literature any adequate study to prove this generally accepted belief. We, therefore, instituted cystoscopy with ureteral catheterization and microscopic examination of the urine from bladder and ureters as a follow-up procedure to determine the effect of operation on the urinary system.

Two hundred patients who had undergone total hysterectomy, either by the abdominal or vaginal route, were studied. They were accepted without reservation if they had previously had a panhysterectomy in our department and would submit to cystoscopy. The investigation was begun in December, 1934, and continued for eight months. The patients were secured from the operative follow-up clinic in gynecology. While some patients declined cystoscopy none were encountered with evidence of serious urinary tract lesions that are not included in this series. The patient with ureterovaginal fistula and stricture, previously mentioned, was not included because the diagnosis was made four months before this study was begun.

The series studied comprised 187 abdominal panhysterectomies, 2 radical abdominal panhysterectomies (Wertheim), and 11 vaginal hysterectomies. With the exception of 4, all were performed by the house staff. Fourteen operators in all participated. Eight of the staff did 5 or less each, 4 did 6 to 25, and 2 did 26 to 80.

The ages of the patients were classified, though there is no particular reason why age should influence injury. It was found that the greatest number, 95, were in the fourth decade of life at the time of operation (Table I). This is in accord with the observation that most major gynecologic procedures are necessary in the late child-bearing age.

TABLE I. AGE OF PATIENTS

1. 21-30	35—17.5%
2. 31-40	95—47.5%
3. 41-50	56—28.0%
4. 51-60	13— 6.5%
5. 61-70	1— 0.5%

Table II lists the major indications for operation. Benign tumors of the uterus lead the list with 96. Inflammatory disease of the adnexa, with 10, is low as a primary indication, but many others presented inflammatory changes though listed under other indications. Injuries of parturition as the chief indication in 70 patients

appears to be a large number. However, marked relaxation of the perineum with injury and infection of the cervix and malposition of the uterus is an important indication for perineal repair and panhysterectomy in the University Hospital Clinic. This, of course, applies to older women who have adequate sized families or are past the child-bearing age.

An analysis of the types of operation done reveals that panhysterectomy alone occurred only 16 times. In all others total hysterectomy was combined with removal of one or more of the adnexa, some type of perineal plastic, or both. All vaginal hysterectomies had adequate perineorrhaphies after reapproximation of the uterine supports and repair of the cystocele. Types of operation are classified in Table III.

Cystoscopy was performed at any time after the six weeks postoperative period. Two-thirds of the entire series were performed in the interval of two to twelve months after operation. The longest interval between operation and cystoscopy was four years and seven months (Table IV). We believe the large number of patients showing residual cystitis (Table VI) is due to the relatively short period between postoperative catheterization and cystoscopy.

TABLE II. MAJOR INDICATIONS

1. Injuries of parturition	70—35.0%
2. Inflammatory disease of adnexa	10— 5.0%
3. Ectopic pregnancy	2— 1.0%
4A. Benign tumors of uterus	96—48.0%
4B. Benign tumors of adnexa	7— 3.5%
5A. Malignant tumors of uterus	3— 1.5%
5B. Malignant tumors of adnexa	3— 1.5%
6. Other indications	9— 4.5%

TABLE III. TYPE OF OPERATION

1. Vaginal hysterectomy plus adnexa	1— 0.5%
2. Vaginal hysterectomy	10— 5.0%
3. Abdominal panhysterectomy alone	16— 8.0%
4. Abdominal panhysterectomy plus plastic	70—35.0%
5. Abdominal panhysterectomy plus adnexa	54—27.0%
6. Abdominal panhysterectomy plus plastic and adnexa	47—23.5%
7. Radical abdominal panhysterectomy (Wertheim)	2— 1.0%

TABLE IV. RELATION OF CYSTOSCOPY TO OPERATION

1. Under two months	25—12.5%
2. Two to six months	80—40.0%
3. Six to twelve months	56—28.0%
4. One to two years	31—15.5%
5. Over two years	8— 4.0%
(Longest interval 4 years 7 months)	

It is well known that lesions of the uterus and adnexa, as well as relaxations due to parturition, are frequently accompanied by urinary symptoms. A study of the history before and after operation reveals an interesting difference in cardinal symptoms. It will be noted in Table V that there was a small but constant reduction in all types of urinary symptoms after operation, although the tendency to infection due to postoperative catheterization is well known. And a comparison

of the number with no postoperative symptoms (Table V) and normal findings on cystoscopy (Table VI) is striking. One hundred forty-five had no symptoms postoperatively and 138 had normal urinary tracts as determined by cystoscopy.

TABLE V. PREOPERATIVE AND POSTOPERATIVE SYMPTOMS

	PREOPERATIVE	POSTOPERATIVE
1. Dysuria	16.5%	11.5%
2. Frequency and urgency	31.0%	21.0%
3. No symptoms	58.5%	72.5%
4. Incontinence	6.0%	3.0%
5. Retention	2.0%	—

TABLE VI. FINDINGS ON CYSTOSCOPY

1. Pyelitis	5— 2.5%
2. Cystitis and trigonitis	35—17.5%
3. Normal	138—69.0%
4. Atony of bladder	15— 7.5%
5. Foreshortened bladder	4— 2.0%
6. Angulation of ureter	3— 1.5%
7. Stricture of ureter	1— 0.5%

All cystoscopic examinations were done in the out-patient department except four that were subsequently admitted for pyelography. No. 21 F. Brown Buerger cystoscopes and No. 5 whistle tip ureteral catheters were employed. Spasm was encountered in 14 cases. Later attempts were successful in 10. Four patients had intravenous pyelograms to rule out stricture. Of these, 3 were normal. One showed a partial obstruction at 5 cm. above the ureterovesical orifice on the left and moderate hydronephrosis. This probably constitutes a ureteral stricture due to operative trauma though a preexisting stricture cannot be ruled out.

We have been impressed by the occasional patient who returned to the follow-up clinic after hysterectomy complaining of urinary frequency and urgency and occasionally of dysuria in whom no evidence of cystitis or urethritis could be found. On cystoscopic examination these patients presented foreshortened bladders with more or less marked lateral bulging. This condition, we believe, results from scar tissue formed under the vesical peritoneum used to cover raw areas. The bladder apparently cannot expand upward as it normally does and a bladder of small capacity is the result. Griffiths, and later, Morris and Brunton, mention various operations that interfere with the filling and ascension of the bladder, but do not describe this condition resulting from hysterectomy. We believe it to be a serious bladder injury, usually due to faulty operative technic and therefore preventable. Foreshortened bladder was encountered in four cases, an incidence of 2 per cent.

Another condition we have observed and have not previously found mentioned is a displacement of the terminal ureter so that it enters the bladder at an angle of approximately 90 degrees. This abnormal

angulation, we believe, is due to fixation of the ureter below the pedicle formed by mass ligation of the base of the broad ligament with the included uterine artery. Theoretically, it may produce hydronephrosis. This marked angulation was observed in three patients. None presented any evidence of hydronephrosis.

It is interesting to note that four patients had double ureters. Three were unilateral and one bilateral. The frequency of this congenital anomaly should be remembered by those doing pelvic surgery.

The sediments from vesical and ureteral specimens of urine were examined in every case. Pyelitis was found in five cases as evidenced by the presence of pus, in the ureteral specimen. Cystitis and trigonitis were determined by appearance of the bladder mucosa and microscopic examination of urinary sediment. Thirty-five patients presented this condition. None of these infections were extensive or acute. Believing these infections probably due to postoperative catheterization or the persistence of a preexisting cystitis, we found that in 25 of the 35 cases with cystitis, cystoscopy had been done within six months after operation, and that 15 were found within three months of operation. In the remaining patients with cystitis some stated that symptoms developed long after operation. These sequelae were probably not due to the operation.

Atony of the bladder was observed in fifteen cases as evidenced by abnormal capacity. This condition was probably present before operation, and due to injuries of parturition. It is possible that later cystoscopy would reveal a return to normal tone in some of these cases. The possibility of operative interference with the nerve supply is to be kept in mind, however.

Finally, 138 patients presented normal urinary systems as determined by cystoscopy and microscopic examination of the urine. This parallels closely the absence of symptoms referable to the urinary tract after operation.

SUMMARY

1. The various types of total hysterectomy are by far the most frequent causes of urinary tract injury.

2. Symptoms referable to injury may be mild or absent for a considerable period of time after operation.

3. Cystoscopic examination of 200 patients who had previously had some type of total hysterectomy was done to determine the incidence of urinary tract sequelae.

4. One patient was found to have a stricture of the terminal ureter with moderate hydronephrosis, and incidence of 0.5 per cent.

5. Four patients presented bladders of small capacity, probably resulting from operation.

6. Three cases with an abnormal angulation of the ureter, possibly due to operation, were found.

7. Fifteen patients showed evidence of atonic bladders.
8. Five patients were found to have pyelitis and 35 to have cystitis.
9. There was a small but constant decrease in all cardinal urinary symptoms after operation.
10. There is a striking analogy between the number having no post-operative urinary symptoms and the number of patients with normal urinary tracts as determined by cystoscopy.

CONCLUSION

We believe cystoscopic examination should be a routine part of the follow-up care in major pelvic surgery. This small series of cases indicates that ureteral or bladder injury is not necessarily a frequent complication of total hysterectomy.

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During the past four years Kovacs has observed 16 cases of gynatresia or stricture of which only 6 were congenital and 13 secondary. The latter type of strictures of the vaginal canal are due to (1) hormonal disturbances, (2) mechanical injuries, (3) chemical and thermic causes, (4) radiation therapy, (5) infections, (6) neoplasms, and (7) foreign bodies.

Hormonal disturbances may result not only in menstrual difficulties, sterility and menopausal troubles but also in local changes in nutrition which are followed by strictures of the vagina. Likewise, changes in the function of the glands of internal secretion may aid the formation of tumors in the genital tract. When neoplasms of unexplained origin are detected, we should think of hormonal abnormalities. The growths in the genital tract which are due to endocrine disturbances heal poorly unless specific therapy is applied. Scar tissue produces either partial or complete atresia of the genitalia. When endocrine therapy is instituted, healing is rapid and without scar formation. Induced abortion may produce atresias in the genital tract and these can be overcome only by extensive operations. The author warns against the indiscriminate application of radium for bleeding from the uterus not due to malignancy. Other forms of therapy applied to the mucous membranes should also be restricted.

The author advocates the use of hormones in all cases of ulcerative processes of the reproductive canal brought about by chemical, thermic, traumatic, or infectious processes, because such treatment will hasten healing and avoid scar formation.

J. P. GREENHILL.

A STATISTICAL ANALYSIS OF THE RECORDS OF PRIMIGRAVIDAS OVER THIRTY-FIVE YEARS OF AGE

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THIS study was undertaken to determine if possible, whether the apprehensions of most patients and some physicians about parturition in the later years of the childbearing cycle, undertaken for the first time, are borne out in actual practice. During the six and one-half years reviewed, there were delivered in the Philadelphia Lying-In Hospital, 13,246 patients. Of this number 113 were having their first labor at age thirty-five or older; an incidence of 0.85 per cent or one in every 117.2 patients. Twenty-two of the 113 were not strictly primigravida, there having been 25 previous pregnancies among them; three being pregnant twice; 21 of which terminated in abortion and 4 in miscarriage.

TABLE I

Philadelphia Lying-In Hospital July 1, 1929 to January 1, 1936			
Total patients delivered		13,246	
Total primigravidas of 35 years or older		113—0.85%	
(One patient in every 117.2)			
White	106	Private	78
Colored	7	Ward	35

Age.—Between the ages of thirty-five and forty there were 98 patients and between forty and forty-five, 15 patients, or a ratio of 6.5:1 in these two groups.

TABLE II. AGES

35 - 21	} 98	40 - 6	} 15
36 - 24		41 - 3	
37 - 20		42 - 2	
38 - 19		43 - 2	
39 - 14		45 - 2	

A complication of pregnancy was noted in 46 or 40.7 per cent of the group. Fifty per cent or half of these had signs or symptoms referable to intoxication or the cardiovascular system.

Labor was complicated in 31 or 27.4 per cent of the patients. The two complications of persistent occipitoposterior and floating head at term accounted for 20 or approximately 66 per cent of those so classified.

Puerperal complications occurred in 35 or 30.9 per cent of these mothers. Sappremia, breast engorgement or postoperative reaction was the complicating factor in 20 or 4/7 of those whose convalescence was not uneventful.

TABLE III. COMPLICATIONS OF PREGNANCY

46 patients—40.7%			
Contracted pelvis	6	Syphilis	2
Cardiac disease	5	Tuberculosis	1
Hypertension	5	Old fracture of pelvis	1
Toxemia	3	Deformed pelvis	1
Preeclampsia	3	Encephalitis lethargica	1
Mild toxemia	3	Psychosis	1
Polyhydramnios	3	Multiple myomectomy	1
Pernicious N. & V.	2	Uterine myomas	1
Edema	2	Placenta previa	1
Antepartum bleeding	2	Cervical polyp	1
		Pyelitis	1

TABLE IV. COMPLICATIONS OF LABOR

31 patients—27.4%	
Persistent occipitoposterior	10
Floating head at term	10
Failure cervical dilatation	3
Moderate postpartum hemorrhage	2
Arrest at midpelvis	2
Contraction ring	1
Disproportion	1
Placenta previa	1
Retained placenta	1

TABLE V. COMPLICATIONS OF PUERPERIUM

35 patients—30.9%			
Sappremia	8	Phlebitis	2
Breast engorgement	6	Cardiac decompensation	2
Postoperative reaction	6	Infected perineum	1
Hypertension	3	Toxemia	1
Pyelitis	3	Peritonitis	1
Bronchopneumonia	2		

Twenty-four patients had no labor, an elective cesarean section being performed before the onset of labor. Thirty-six had less than ten hours. Forty had less than twenty hours. Thirteen had labors in excess of twenty hours; the longest seventy-three hours twenty minutes, but doubtless in many of these the presence of rhythmic hard contractions was intermittent and not constant. The average length of labor for the entire group was eleven hours. Excluding the 24 who had no labor, the average was 13.9 hours.

Of the 116 infants, 103 were vertex presentations; 10 breech; 1 transverse, and 2 undiagnosed at the onset of labor. Occiput anterior in 59; transverse in 12; posterior in 18; and positive position unknown in 14.

Delivery was spontaneous in 8 labors; by forceps in 61, of which 44 were low forceps and 17 midforceps applications. Cesarean section was performed on 28 patients; internal podalic version in 10; breech extraction in 8; and the extraction of a transverse presentation in 1.

The combined operative incidence was 92.9 per cent.

TABLE VI

TOTAL NUMBER	HOURS LABOR	TOTAL NUMBER	HOURS LABOR
24	0	6	15+
1	2+	3	16+
6	3+	5	17+
4	4+	5	18+
8	5+	1	19+
1	6+	3	20+
8	7+	2	23+
3	8+	1	24+
5	9+	1	25+
4	10+	2	31+
6	11+	1	36+
4	12+	1	42+
1	13+	1	46+
5	14+	1	73+
Average (11 hours for 113) (13.9 hours for 89)			

TABLE VII. OPERATIVE INCIDENCE

105 patients—92.9%	
Forceps	52.2%
Cesarean	24.7%
Version	8.8%
Breech	6.1%

Episiotomy was performed 40 times; 1° laceration sustained 9 times; 2° laceration, 16 times; 3° laceration, 3 times.

TABLE VIII. LACERATIONS

1°	9
2°	16
3°	3
Episiotomy	40

TABLE IX. ANALGESIA

Nembutal and scopolamine	27
Morphine and scopolamine	18
Morphine	9
Sodium amytal	5
Barbital	2
Codeine	1
Nembutal and codeine	1
Scopolamine	2
Nembutal	1
None	45
Gwathmey { alone	2
combined	6

Analgesia in one form or another was given to 68 patients; 45 of these women were allowed to continue spontaneously, unaided through the first stage of labor.

All but four of the deliveries were accomplished under anesthesia; of these, 2 were precipitate and 2 were at the end of three- and four-hour labors, with small infants weighing under four pounds.

TABLE X. ANESTHESIA

Ether	55
Gas ether	38
Gas	8
Gas oxygen	6
Chloroform	2
None	4

Twenty-eight elective cesarean sections were done, or an incidence of 24.7 per cent. Contracted pelvis, failure of the cervix to dilate, floating head at term in a primigravida, or cardiac disease, were the indications in 18 or 64 per cent of the patients.

TABLE XI. CESAREAN SECTION—28 OR 24.7%

Failure of cervical dilatation	4
Floating head in primigravida	4
Contracted pelvis	7
Cardiovascular disease	3
Elderly primigravida	3
Uterine myomas	2
Placenta previa	2
Toxemia	1
Tuberculosis; disproportion	1
Section and sterilization	1

In 113 pregnancies there were three sets of twins or a total of 116 infants. Of these, 112 were born alive and 4 were stillborn. Females predominated 65:51. Fifteen babies weighed under 5 pounds and five over 8 pounds. Six were premature.

TABLE XII

WT. OF INFANTS	TOTAL NUMBER
2 pounds plus	3
3 pounds plus	6
4 pounds plus	6
5 pounds plus	16
6 pounds plus	24
7 pounds plus	42
8 pounds plus	14
9 pounds plus	5

Twenty-nine mothers were morbid, or 25.6 per cent. Breast engorgement, postoperative reaction, sapremia, and pyelitis accounted for 22 or 75.8 per cent.

Two mothers in this series died, or 1.76 per cent; one from shock and cardiac failure following a version after eighteen hours of labor. Baby

weighed 7 pounds and 10 ounces. A severe 3° laceration was sustained in this delivery. The other died from postoperative peritonitis following an elective cesarean section, before the onset of labor.

TABLE XIII. MATERNAL MORBIDITY

29 patients—25.6%	
Breast engorgement	6
Postoperative reaction	6
Sapremia	7
Pyelitis	3
Bronchopneumonia	2
Infected perineum	1
Toxemia	1
Endometritis	1
Peritonitis	1
Phlebitis	1

TABLE XIV. MATERNAL MORTALITY

2 patients—1.76%	
Shock; cardiac failure	1
Postoperative peritonitis	1

Four infants were morbid or 3.45 per cent.

TABLE XV. FETAL MORBIDITY

4 infants—3.45%	
Prematurity and pneumonia	1
Dehydration	1
Spina bifida and hydrocephalus	1
Cause unknown	1

The combined fetal mortality rate was 8.62 per cent or 10 infants. Of these, 4 were stillborn; 4 were premature, and 1 was deformed. One died

TABLE XVI. FETAL MORTALITY

10 infants—8.62%	
Stillborn	4
Prematurity	3
Spina bifida and hydrocephalus	1
Breech, immature	1
Intracranial hemorrhage	1

TABLE XVII. COMPARISON OF THIS SERIES TO HOSPITAL IN GENERAL

THIS SERIES		
Complications of pregnancy	40.7	18.6
Complications of labor	27.4	14.3
Complications of puerperium	30.9	21.6
Maternal morbidity	25.6	19.8
Maternal mortality	1.76	0.57
Fetal morbidity	3.45	
Fetal mortality {	Uncorrected	8.62
	Corrected	0.86
		2.60

same result [Friedman + (weak) and Aschheim-Zondek - (slip)] may be yielded by the girl around the time of puberty in cases of rape and assault, and in these a negative is likely to be the correct interpretation. It is more difficult to explain away the Friedman negative and Aschheim-Zondek positive disagreement. If one must choose between the + and the -, then it is safe, as a rule, to prefer the +. Refractory rabbits are not uncommon. But the + is not always correct as is seen in the first confirmation.

TABLE II. DISAGREEMENT BETWEEN FRIEDMAN AND ASCHHEIM-ZONDEK TESTS

NO. OF CASES	FRIEDMAN	ASCHHEIM-ZONDEK	CONFIRMATIONS
5	-	+	<ol style="list-style-type: none"> 1. Friedman - correct, yet every one of the 5 mice in the A-Z gave a strong +. Single woman greatly fearing pregnancy. Last menstrual period 6 weeks ago. 2. A-Z + correct. Thought to be a case of ectopic gestation. Operation revealed uterine pregnancy. Fetus alive at time of test. Died later when A-Z repeated gave -. 3. A-Z + correct. 4. A-Z + correct. Patient 1-2 months pregnant at time of test.
4	+	-	<ol style="list-style-type: none"> 1. A-Z - correct. Friedman repeated 1 week later gave -. 2. A-Z - correct. Operation disclosed fibroid. Friedman was rather indefinite +, a - report issued.
11	+	-(slip)	<ol style="list-style-type: none"> 1. Friedman + correct. Patient 3 weeks pregnant at time of test.
3	+(weak)	-(slip)	<ol style="list-style-type: none"> 1. A-Z - correct (Friedman first rabbit -?; second +?). Young single girl. 2. A-Z - correct. Repeated later gave +. Medico-legal case of girl aged 15½, 4½ months pregnant at time of test. 3. Case of incomplete abortion with greatly degenerated decidual tissue and a dermoid in the left ovary.

TOXIC SPECIMENS

In thirty-four cases the test was not completed for the reason that the injections killed the animals concerned. In two of these the urine on receipt was of a bright green color, and enquiry elicited the fact that brilliant green had been painted upon the patient's cervix some time before the specimen was taken. All attempts to remove this from the specimen failed, and the injections were almost immediately lethal. As has been noticed frequently, many of the specimens that fall into this uncompleted class are derived from single women who have reason to wish to avoid pregnancy. It would seem that quite commonly some attempted chemical interference with pregnancy is the reason for the lethal properties of the specimen.

to the standards used this result must be returned as a negative, yet the vaginal and uterine enlargement indicated that in the specimen the concentration of hormones was unusually high and that this might mean one of several things: e.g. very early pregnancy, early pregnancy in a woman with exceptionally low hormone concentration, menopausal state, incipient menstruation (after a phase of amenorrhea), fairly recent death of the ovum, lactation, or some general endocrine disturbance not connected with pregnancy. (Experience has shown, also, that this uterine and vaginal enlargement is to be expected and disregarded in mice that are too large or too old and which should not have been used in these tests.) In these cases the practitioner is advised to have the test repeated in about ten days' time if doubt persists.

Of the conditions which are known to be associated with this uterine enlargement, early pregnancy, of course, is the only one which, if the test were repeated, would contradict the negative result first obtained. Of the 573 cases in which this slip was attached to the report, no confirmation was received in respect of 406. In 151 the negative result was found to be in harmony with the subsequent clinical history, while in 16 pregnancy had existed at the time of the test. For the reason that, in the reports issued in these cases, it was stated that early pregnancy could not be excluded, these results are not regarded as errors. Though the practitioner who receives such a result is naturally inclined to be irritated, for he has such implicit faith in these tests as to demand a plain unqualified positive or negative, it is our practice to furnish him with a full and complete statement of the result obtained. It is for him to make the diagnosis. The report issued from this Laboratory is but one of many factors that he must evaluate in arriving at his diagnosis.

A review of the records of all the Aschheim-Zondek tests carried out here during the last six years makes it quite clear that the concentration of gonadotropic hormones in different women during early pregnancy varies very widely. Very rarely is it such as to leave the mice completely unaffected when a false negative is obtained. Less rarely is it so low as to produce only uterine and vaginal enlargement, and without a knowledge of the age and history of the patient, all that can be done is to recommend that the test be repeated later.

In 23 cases the Friedman and Aschheim-Zondek tests disagreed. These disagreements provoke much anxiety and dissatisfaction. The disagreement between the Friedman + and + (weak) and the Aschheim-Zondek - and - (slip) is more apparent than real. Under the conditions that obtain here the rabbit picks up a concentration of gonadotropic hormones to give a +, while in the Aschheim-Zondek a - or - (slip) is obtained. This is the result that is to be expected in very early pregnancy, in pregnancy of four or six months' duration, in cases in which the hormone concentration is unusually low and in cases of recent fetal death. The

x-ray examination, pregnancy had been stated not to exist, positives, which were later confirmed, were obtained.

One point that may be of interest to others who are carrying out these tests is that about 1 in every 100 packages containing specimens is broken in the post. In order to cope with this misfortune, a small hand press was devised. Into this, the cotton wool, cardboard, and correspondence is placed and the fluid expressed therefrom. Such treatment in no way affects the properties of the specimen.

TESTS IN RELATION TO THE AGE OF THE PATIENT

The practitioner is requested, when sending in a specimen, to state the age of the patient, the date of the last menstrual period, and any other detail of the clinical history that he thinks might be of help in the interpretation of the result obtained. In 2,375 cases the age of the patient was given. It ranged from thirteen to sixty-five over the following distribution:

AGE	13	14	15	16	17	18	19	20	21	22	23	24	25
NO. OF TESTS	2	8	11	21	24	29	40	53	78	75	77	98	107
AGE	26	27	28	29	30	31	32	33	34	35	36	37	38
NO. OF TESTS	103	116	96	29	115	79	112	77	85	97	83	60	63
AGE	39	40	41	42	43	44	45	46	47	48	49	50	51
NO. OF TESTS	63	95	59	72	58	48	50	41	21	19	18	10	6
AGE	52	54	65										
NO. OF TESTS	4	1	1										

This range covers the whole of the ordinary reproductive phase of the individual life with slight extensions at both ends. The number of tests rises sharply with the age of the subject to reach a peak at 24 to 27. The fewness of the specimens from women of twenty-nine years seems to require some explanation. From a second peak at 32 the number falls more or less gently to the end.

Of the two cases in the thirteen age group, one was positive and was of interest in that the doctor reported that the hymen remained imperforate. Positives were given by two of the girls of fourteen; 5 of those of fifteen; 3 of the sixteen class, together with 1 which turned out to be a hydatidiform mole; 10 of those aged seventeen. At the other end of the scale, every one of the fifty age class gave a negative result; of the fifty-one, one was a mole and the rest negative; of the fifty-two, one was a mole, one positive and one negative. The woman aged fifty-four years was negative, as was also the woman of sixty-five who was shown to have a very large ovarian cyst.

DISTRIBUTION OF TESTS IN RELATION TO THE DATE OF THE LAST MENSTRUAL PERIOD

In 2,049 cases the date of the last menstrual period was recorded among the particulars sent with the specimen. It will be seen that in 97 cases no menstrual period had yet been missed. These are the cases

DILUTION TESTS

In those cases in which hydatidiform mole or chorionepithelioma is suspected, in addition to the ordinary Aschheim-Zondek, in which prepared undiluted urine is used, additional groups of mice are injected with urine diluted 9 and 99 times its own volume with distilled water. Experience has shown that while normal pregnancy can give a positive with undiluted urine and with the 1/10 dilution, it is exceedingly rare for it to do so with the 1/100; in fact, so rare that a positive 1/100 is regarded as being strongly indicative of mole or chorionepithelioma. In cases in which the mole has been expelled or removed, these tests are repeated at monthly, and later at bimonthly, intervals in order that recurrence may be recognized. There were 171 such dilution tests carried out during the year. It is the rule that a hydatidiform mole or chorionepithelioma gives + + +, that after removal there is a gradual and progressive swing toward ---. This result was obtained in some cases as early as one week after the evacuation, but this is rare; usually this result is obtained about three months afterward. In one case a + --, in the absence of recurrence, was obtained as late as one year after removal.

Urines from 14 males were examined by these dilution tests in cases in which malignant diseases of the testis were suspected or in which a malignant tumor had been removed.

Urine from treated cases of seminoma persistently gave negative results. In two cases only were positive results obtained. In one +, - (slip), - (slip), orchidectomy revealed an embryonal-celled carcinoma; in the other + (weak), -, -, a carcinoma of the testis was found on operation.

GENERAL

In addition to the cases of particular interest so far mentioned, it is perhaps advisable to record that negatives, later confirmed, were obtained in cases of tuberculous peritonitis, large cyst in the broad ligament, parovarian cyst, chronic salpingitis, torsion of the fallopian tube, endometrioma of left ovary, and following the removal of a luteinoma of the ovary, as well as in several instances of carneous mole and of pseudo-eyes. Positives, later confirmed, were obtained in a case of ovulation without menstruation, in another in which there was very severe hydramnios in a mental patient previously sterilized, and in others in which deep x-ray therapy had previously been exhibited. In one case in which mole was suspected because of the disproportionate size of the uterus, a + -- was obtained in the dilution test, and the final diagnosis was twins. Positives were also obtained in cases in which patients had been married for twelve, fifteen, and sixteen years, respectively, without having produced any issue during this time. On the other hand, a positive was also obtained in the case of a woman who had been married exactly twenty days prior to the test. In two cases in which, following

From this point onward the reason for the test would seem to change somewhat. It becomes more and more a matter of differential diagnosis and less a diagnosis of pregnancy before the clinical picture becomes clear. Fetal death is a much more frequent cause, owing to the fact that the enlargement of the uterus has fallen out of step with

TABLE IV. QUANTITATIVE ESTIMATIONS

DOCTORS' DIAGNOSIS AND DEMANDS	ESTRIN INTERNA- TIONAL UNITS PER LITER	GONADO- TROPIC HORMONE RAT UNITS PER LITER	MALE HOR- MONE INTERNA- TIONAL UNITS PER LITER	
1. Fluid from breast cyst. Estrin estimation	30 in the 12 c.c.	-	-	Freed's method for blood because of large amount of protein contained in the fluid
2. Granulosa celled tumor of left ovary. 10 c.c. of urine taken just before operation	= 50			
30 c.c. taken 24 hr. after operation. Estrin estimation	= 33			
3. Endocrine disturbance, obesity, amenorrhea, milky secretion in breasts and bluing of vulva. Estrin and gonadotropic es- timation	12	> 1		Aschheim-Zondek
4. Myxedema. Estrin and gonadotropic es- timation	> 3	> 1		
5. Estrin deficiency. Estrin estimation	10			
6. Persistent amenorrhea. Estrin and gonadotropic es- timation	2	12		
7. Amenorrhea. Girl of 15. Blood estrin Urine estrin	app. 2 in 40 c.c. 8			
8. Irregular menstruation. Estrin and gonadotropic es- timation	12	2.5		
9. ? Estrin and gonadotropic es- timation	10	< 1		
10. ? Estrin and gonadotropic es- timation	11	2.3		
11. Amenorrhea with hirsutes. Male hormone			36	No free ♂ hormone
12. Hermaphrodite. Estrin and male hormone	30		120	
13. Seminoma testis (postop- erative). Male hormone estimation		< 1		

in which, commonly, medicolegal interests are involved or in which the earliest possible diagnosis of pregnancy following exposure is required for the reason that therapeutic abortion has to be considered. In a considerable number of these tests, the question of ectopic gestation had arisen. But undoubtedly the number includes a great many which can

TABLE III

Weeks after last men- strual period	1	2	3	4	5	6	7	8						
No. of cases	12	22	21	42	266	319	169	373						
Positive	2	9	9	15	107	174	98	224						
Confirmed	0	3	4	5	41	51	23	71						
Negative	10	13	12	27	109	145	71	149						
Confirmed	4	3	5	13	39	43	20	38						
Errors	-	2	-	1	-	-	1	2						
Weeks after last men- strual period	9	10	11	12	13	14	15	16						
No. of cases	146	105	57	225	31	35	10	86						
Positive	107	69	33	128	17	16	8	54						
Confirmed	35	17	10	38	2	2	1	15						
Negative	39	36	24	97	14	19	2	32						
Confirmed	12	8	10	26	4	4	1	8						
Errors	-	-	-	-	-	2	-	1						
Weeks after last men- strual period	17	18	19	20	21	22	23	24						
No. of cases	14	26	3	47	3	9	0	34						
Positive	8	16	0	27	2	7	0	13						
Confirmed	1	5	0	6	1	3	0	7						
Negative	6	10	3	20	1	2	0	21						
Confirmed	2	3	0	5	1	0	0	3						
Errors	-	-	1	-	-	-	-	3						
Weeks after last men- strual period	26	28	29	30	32	33	34	35	36	40	44	48	52	104
No. of cases	1	19	1	1	7	2	2	1	1	2	1	1	4	1
Positive	0	11	0	0	0	2	0	0	1	0	0	1	2	0
Confirmed	0	4	0	0	0	0	0	0	0	0	0	0	0	0
Negative	1	8	1	1	7	0	2	1	0	2	1	0	2	1
Confirmed	0	2	0	1	1	0	1	0	0	0	0	0	1	1
Errors	-	-	-	-	-	-	-	-	-	-	-	-	-	-

only be regarded as testimony to the doctor's faith in the almost magical efficacy of these tests. In two cases it was actually discovered on enquiry that fertilization, had it occurred, had taken place no more than twelve hours previously. Negative results are almost twice as frequent as are positives in specimens taken up to four weeks following the last menstrual period. This is as would be expected. It is indeed somewhat surprising that only 3 of the errors fall into this group.

The cases in which one period only had been missed (i.e., five to eight weeks after the last menstrual period) are the most numerous, constituting no less than 1,127 out of 2049 cases. This is quite as it should be, for it is here that the pregnancy diagnosis tests should and do provide the greatest help. In this group the positives outnumber the negatives, 603 : 474, and only 3 errors require to be recorded.

ON THE INACTIVATION OF ESTRONE, ESTRADIOL, AND THEIR MONOBENZOATES IN THE ORGANISM

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IN ORDER to understand the mechanism of the action of estrogenic compounds, especially as to their therapeutic effects in human subjects, it is of considerable importance to know the fate of the estrogenic substances in the body. Our investigations on this subject consist of experiments with human beings as well as with animals. Those carried out with human subjects will be published elsewhere; in this paper, only the results obtained from experiments with animals will be recorded.

PREVIOUS INVESTIGATIONS

Some years ago Frank, Goldberger, and Spielman (1932) observed that half hourly blood samples taken from isolated adult rabbits, into which 2,000 M.U. of estrogenic hormone were injected intravenously in one dose, yielded only 1 M.U. in 4 c.c. of serum during the first hour and less thereafter. A rabbit injected with 3,000 M.U. and killed twenty-four hours later by bleeding showed less than 2 M.U. in the total blood volume. Fee, Marrian and Parkes (1929) using the heart-lung-kidney preparation, after adding 200 "mouse units" of estrone to about 500 c.c. of blood in circulation, could detect estrone in none of the organs perfused in this preparation. These authors think it probable that the hormone is destroyed by oxidation while passing through the lungs.

In an extensive investigation on the fate of estrogenic substances in the animal organism, Zondek (1934) made the following observations: After administering estrone subcutaneously to immature rats in amounts up to 20,000 M.U., no hormone at all was excreted in the urine. If amounts up to 40,000 M.U. of estrone were injected subcutaneously into immature rats and the animals were killed at different intervals (three to seventy-two hours) afterward, no more than 2 per cent could be recovered after neutral and 20 per cent after acid extraction. A possible conversion of estrone into estriol could not be proved.

When, however, immature rats received estrone benzoate injected subcutaneously, forty-eight hours after the injection, 80 to 90 per cent of the amount injected could be recovered from the extraction of the entire rat. According to Zondek this phenomenon explains Butenandt's (1930) finding of the protracted estrogenic action of estrone benzoate and confirms his view that the action of benzoate is due to its being slowly hydrolyzed in the body. From the fact that estrone benzoate is still active in the organism under circumstances in which estrone is not, this author discusses the possibility that the inactivating process starts at the phenolic hydroxyl group of the estrone molecule which in estrone benzoate is protected by the esterification with benzoic acid. From in vitro experiments, he ascertained that the liver probably plays a part in the inactivation; for, after shaking estrone with mashed liver of immature rats at 37° C., a strong inactivating effect could be observed in most cases. This effect was not obtained when the mashed liver was heated beforehand to 70° C.

the duration of pregnancy. The positive results continue to outnumber the negatives until the last two groups are reached, and, as would be expected, in the last group (26 to 104 weeks after the last menstrual period) the negatives greatly preponderate.

QUANTITATIVE ESTIMATIONS

During the latter part of the year, in response to demands made upon the Laboratory, arrangements were completed whereby quantitative estimations of estrin, gonadotropic and male hormones in blood and urine could be undertaken. Though in my view it is as yet doubtful that the information that this Laboratory can supply can be of any considerable value to the clinician, certainly anything that can aid in the advancement of our knowledge concerning these hormones must eagerly be undertaken in order that the time may come when endocrine therapy may be securely based upon a sufficient body of accurate knowledge. At the moment the results of these estimations possess an interest which is mainly academic. For the extraction from the urine of estrin and male hormone a modification of the Gallagher and Koch method is used; for the gonadotropic hormone the alcohol precipitation method is employed; for blood estrin and gonadotropic extraction Freed's method is used. Groups of ovariectomized mice are used in the assays of estrin; capons for the male hormone; and immature female rats for the gonadotropic hormones. The amounts of estrin and male hormone are given in international units per liter; that of gonadotropic hormones in rats units per liter, the rat unit being that amount required to produce a 33 mg. ovary in an immature female rat of 40 gm. body weight under the conditions that obtain here.

dredth of the activity of estrone. On the other hand, the potency of the hydrate in regard to its ability to cause opening of the vagina of infantile rats is much greater than that of estrone. In order to determine whether estriol is present, two units of the estrogenic hormone from the urine, in solution in oil, were injected twice daily for two and one-half days, into a number of immature rats of the same age and weight. Control animals received two injections of two units each of crystalline estrone dissolved in oil. Since opening of the vagina occurred at the same time in most of the animals, the absence of significant amounts of estrone hydrate was proved.

B. CONTENT OF ESTROGENIC HORMONE IN THE WHOLE ORGANISM AFTER INJECTION OF ESTRONE

Since the urine and feces yielded only very small amounts of the injected estrone, the question arose as to whether estrogenic substance could still be detected in the body after the injections, and, if so, where. To solve this problem it was felt that a quantitative hormone extraction of the animal's entire body was of decided importance. Inasmuch as before this, we had performed only a few similar experiments we, therefore, at the beginning of this investigation, used three different methods of extraction: (1) Extraction with benzene after immediately adding acid. (2) Alcohol extraction: (a) without subsequent acid hydrolysis, and (b) with subsequent extraction in acid medium. (3) Benzene extraction after drying the minced animal with sodium sulphate. In all three extraction methods the whole animal was first ground in a mincing mill to a mash. The urine and feces collected from the beginning of the experiment were added to this. The estrogenic activity of the extracts obtained by these three different methods was all assayed in the usual manner in castrated mice.

Method 1.—The mash was mixed with water to a total weight of 500 gm. After adding 75 c.c. of 25 per cent aqueous hydrochloric acid and 200 c.c. of benzene, the mixture was refluxed in a round-bottomed flask on a water-bath; the benzene being renewed twice during the extraction. The combined benzene extracts were first washed with water, until the wash water had a neutral reaction, and then evaporated in vacuo. The residue was dissolved in oil and assayed in ovariectomized mice.

Method 2.—The mash was mechanically shaken for twenty-four hours in 4 volumes of 96 per cent alcohol and centrifuged. The supernatant alcohol was passed off and the remainder was shaken twice more with 500 c.c. of 70 per cent alcohol. The combined alcohol extracts were evaporated to dryness; the residue treated with a small amount of alcohol, and centrifuged. One part of this extract was used for testing (Method 2a); the remaining part was suspended in water. To each cubic centimeter of liquid, 150 c.c. of 25 per cent hydrochloric acid were added and extraction was performed for 3 periods of four hours each with one-third volume of benzene (the benzene being renewed twice). The combined benzene extracts were washed and evaporated.

Our investigations were carried out with pure estrone* and estradiol; and with the benzoic ester of estrone and the monobenzoic ester of estradiol. All crystalline hormones were injected subcutaneously, dissolved in 1 c.c. of olive oil. As test animals we used mature female rats weighing between 150 and 200 gm. At the end of the experiment these animals were killed by a blow on the head.

A. EXCRETION OF ESTRONE IN URINE AND IN FECES OF MATURE FEMALE RATS AFTER SUBCUTANEOUS ESTRONE ADMINISTRATION

In the first experiments the excretion of estrone in the urine and feces of rats was investigated after injection of relatively large quantities of the hormone. Two test animals received subcutaneously 25,000 R. U. dissolved in oil. The urine and feces were collected during four days after the injection and worked up separately. The urine, including the wash water with which the cage had been rinsed, was refluxed with benzene on a water-bath for three periods of four hours each, the benzene being renewed each time. To each liter of residual water-urine mixture, 150 c.c. of 25 per cent hydrochloric acid were added. The acid mixture was extracted with benzene three times. The acid benzene extracts were united and washed with water. Both the neutral and acid benzene extracts were then evaporated and the residues dissolved in oil and tested for their estrogenic hormone content in ovariectomized mice (de Jongh and others, 1932). The neutral extract proved to contain 150 and 50 estrogenic units, respectively, while in the acid extracts in both cases, less than 50 estrogenic units could be detected. In the urine collected during four succeeding days after the injection, the maximum found was 150 units, that is 0.6 per cent of the amount of estrone injected.

The feces proved to contain 100 and 750 units, respectively; extraction was carried out in the acid medium in the manner described above. Although not more than 3 per cent of the injected amount could be extracted from the feces, this is still more estrogenic substance than is excreted in the urine. After this, the urine and feces were collected during another four days. In only one case could more than 50 M.U. be detected in the urine or feces. (In the urine of the second test animal 100 M.U. of estrogenic substance was found.) It was evident that after receiving injections of estrone, rats excrete considerably less estrogenic substance in the urine and feces than we found in our experiments with human beings.

Now the possibility presented itself that the injected estrone might be excreted in the urine as its hydrate, since it is known that the estrogenic activity of estrone hydrate (estriol) is only about one one-hun-

*We wish to thank the N. V. Organon Company for their kindness in supplying us with these substances.

from intracranial hemorrhage following an "emergency" version delivery, forceps having failed. The preventable obstetric fetal mortality is therefore 0.86 per cent.

CONCLUSIONS

A comparison of this series of 113 patients with the total of 13,246 prompts the following conclusions:

1. Complications of pregnancy will occur considerably more often.
2. Complications of labor will be more frequent.
3. Complications of the puerperium will be encountered a trifle more often.
4. The operative incidence will and should be considerably higher than in the younger primigravida group.
5. The cesarean section incidence from five to six times as great.
6. Maternal morbidity 5 per cent higher.
7. Maternal mortality over three times as great.
8. Fetal mortality one-third as great.

THE EFFECT OF ARTIFICIAL PSEUDOMENSTRUATION AND MENSTRUATION ON THE INCREASED ELIMINATION OF PROLAN A IN THE ABSENCE OF OVARIAN FUNCTION

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IN 1930¹ I demonstrated the fact that there is an increased elimination of follicle-producing hormone in the urine in the absence of the ovarian function (more than 100 mouse units prolan A per liter). At that time I also showed an increased elimination of hormone in 13 out of 15 (i.e., in 86.6 per cent) castrated women between twenty and fifty-two years of age. Ten days after castration follicle-producing hormone is present in the urine. I could also demonstrate the existence of the same phenomenon during the period when the ovary normally ceases to function, i.e., at the climacteric. The latter has three differing hormonal phases, the last of them being the polyprolanal phase. If ovarian function stops in a woman of the procreative age, which is shown clinically by a long amenorrhea, this disturbance is characterized by an increased elimination of prolan A. These findings have been studied and verified by many authors.

In the following investigations, the question is whether the increased elimination of prolan A might be influenced by producing artificial menstruation. Examinations were made in cases of primary

Method 3.—The mash was mixed with an equal weight of anhydrous sodium sulphate and allowed to stand overnight. The next day the hard mass was powdered and boiled using reflux with benzene three times during four hours, the benzene being renewed each time. The combined benzene extracts were evaporated to dryness.

ANIMAL EXPERIMENTS

First the content of estrogenic material in the normal rat was determined. Extractions were carried out with three female rats, weighing between 170 and 210 gm., according to Method 3. The neutral extraction was followed by an acid one; after neutral extraction, 500 c.c. of 4 per cent hydrochloric acid were added to the residue and the mixture was boiled with benzene. None of the extracts, whether neutral or acid, showed any trace of estrogenic activity working on the assumption that 50 M.U. might be present in the whole animal. The amounts collected from the whole animal at different intervals after injections of estrone and estradiol are summarized in Table I.

a. *Free Estrone and Estradiol.*—Forty-eight hours after the injection of estrone and estradiol, the hormone content of the body, with one exception, was less than 10 per cent of the amount injected. Six hours after the hormone injections, an average of only 20 per cent of the amount of hormone injected could be recovered. However, one and two hours after the injections, as much as 70 to 80 per cent was still present. With the three methods already described, the same values were obtained. This proves that the hormones administered were not converted into a combined form, i.e., in a form in which they occur in human urine. The experiments with 1,000 and 10,000 M.U. gave exactly the same results.

b. *Investigations With Benzoate.*—With the benzoates the result was different. Forty-eight hours afterward, between 20 to 60 per cent was still recovered; approximately the same values were obtained twenty-four hours afterward (40 to 70 per cent). One to two hours after the injections, practically the total amount of hormone injected could be detected.

These results agree with the well-known protracted activity of the benzoate esters. In our experiments with hormone benzoates, we obtained the same quantities of hormone by all methods with and without hydrolysis. Since we know that the free hormone in equal quantity exerts an activity four times stronger than the corresponding benzoate, the question may arise whether a liberation of free estrone could have occurred during extraction, or in the body of the animal after administration of estrone benzoate. This, furthermore, would have accounted for a high estrogenic activity of the extract in spite of the loss of 75 per cent of the injected estrone benzoate.

A closer investigation showed that under the conditions chosen, the benzoic esters are not saponified in acid medium. In the first place, both esters are more easily saponified in alkaline than in acid medium; moreover, as in our Methods 1 and 2b, heating had only begun after the addition of benzene, the ester had passed into it already and so escaped hydrolysis. The following experiment proves this to be the case.

There were 5,000 M.U. of estrone benzoate dissolved in 10 c.c. of oil. To 4 c.c. of this oily solution (~2,000 M.U.) were added 50 c.c. of 96 per cent alcohol and 2 gm. of potassium hydroxide dissolved in a little water. After refluxing for four hours, the mixture was worked up in the usual way and the quantity of estrogenic material estimated biologically. As this amounted to 8,000 M.U. a complete saponification had taken place in this alkaline solution. Another 4 c.c. of the oil was refluxed with 500 c.c.

TABLE I. RECOVERED HORMONE QUANTITIES IN THE TOTAL ANIMAL IN DIFFERENT INTERVALS AFTER INJECTION*

NO.	ESTROGENIC HORMONE	QUANTITIES INJECTED SUBST.		METHOD OF EXTRAC- TION	KILLED AFTER	HORMONE M.U.	RE- COVERED PER- CENTAGE
		M.U.	MG.				
10	Estrone	1,000	0.1	I	48 Hr.	100	10
12	Estrone	1,000	0.1	III	48 Hr.	100	10
19	Estrone	10,000	1.0	IIa	48 Hr.	150	1.5
30	Estrone	10,000	1.0	III	48 Hr.	100	10
31	Estrone	10,000	1.0	III	48 Hr.	700	7
32	Estrone	10,000	1.0	III	48 Hr.	300	3
20	Estrone	1,000	0.1	IIa	6 Hr.	300	30
21	Estrone	1,000	0.1	IIa	6 Hr.	200-300	20-30
79	Estrone	10,000	1.0	I	6 Hr.	1,600	16
80	Estrone	10,000	1.0	I	6 Hr.	2,000	20
81	Estrone	10,000	1.0	I	6 Hr.	1,500	15
1	Estrone	10,000	1.0	I	1-2 Hr.	7,000	70
2	Estrone	10,000	1.0	IIa	1-2 Hr.	7,000	70
				IIb	1-2 Hr.	7,000	70
3	Estrone	10,000	1.0	III	1-2 Hr.	1,000	100
3	Estrone	1,000	0.1	I	1-2 Hr.	750	75
4	Estrone	1,000	0.1	III	1-2 Hr.	800	80
18	Estradiol	1,000	0.05	IIa	6 Hr.	200	20
19	Estradiol	1,000	0.05	IIa	6 Hr.	100	10
4	Estradiol	1,000	0.05	I	1-2 Hr.	700	70
5	Estradiol	1,000	0.05	IIa	1-2 Hr.	600	60
	Estradiol	1,000	0.05	IIb	1-2 Hr.	800	80
6	Estradiol	1,000	0.05	III	1-2 Hr.	750	75
26	Estradiol	1,000	0.05	IIa	1-2 Hr.	700	70
40	Estrone benz.	1,000	0.4	III	48 Hr.	600	60
51	Estrone benz.	2,000	0.8	III	48 Hr.	400	20
52	Estrone benz.		0.8	III	48 Hr.	500	25
39	Estrone benz.	1,000	0.4	IIa	24 Hr.	700	70
42	Estrone benz.	1,000	0.4	IIa	24 Hr.	500-600	50-60
15	Estrone benz.	1,000	0.4	I	1-2 Hr.	800	80
16	Estrone benz.	1,000	0.4	IIa	1-2 Hr.	1,000	100
				IIb	1-2 Hr.	1,000	100
17	Estrone benz.	1,000	0.4	III	1-2 Hr.	750	75
41	Estradiol-mono- benzoate	1,000	0.125	III	48 Hr.	200	20
38	Estradiol-mono- benzoate	1,000	0.125	IIa	24 Hr.	600	60
43	Estradiol-mono- benzoate	1,000	0.125	IIa	24 Hr.	500	40
7	Estradiol-mono- benzoate	1,000	0.125	I	1-2 Hr.	750	75
8	Estradiol-mono- benzoate	1,000	0.125	IIa	1-2 Hr.	900	90
9	Estradiol-mono- benzoate	1,000	0.125	III	1-2 Hr.	800	80

*Each dosage was tested in 3 mice (12-24 mice were used) for the complete assaying of each preparation.

of a 4 per cent aqueous solution of hydrochloric acid and benzene for three periods of four hours, the benzene being renewed twice. The combined benzene extracts were washed, evaporated, and the dry residue assayed. This proved to contain 2,000 M.U. of estrogenic hormone only. Under the above-mentioned conditions in this acid medium, no saponification had taken place at all. Repeated experiments yielded the same result.

The question now arises as to where and in what form the hormone which was recovered from the animal's body is found. This question is of great importance, particularly in regard to the benzoate. There are two possibilities: (1) the hormone is still in the original place of injection, i.e., it has not been absorbed, and (2) the hormone was absorbed immediately but is circulating in the body or temporarily has been stored somewhere in the body. In an attempt to find an answer to this question, the following experiment was carried out. There were 10,000 M.U. of estrone injected into a rat, and one hour later the animal was killed and divided into two parts. The part containing the site of injection weighed 48 gm.; the other part, 102 gm. Both parts were extracted according to Method 2a. In the former part (that with the site of injection), 8,000 M.U. of estrone were found; in the latter, 1,500 M.U. From these facts we may conclude that after one hour, only a small part of the estrone has been absorbed. Another rat received 10,000 M.U. of estrone and was killed one hour after the injection. But in this case the oil at the site of injection was removed with a piece of cotton wool and the area washed with ether. The piece of skin at the site of injection was removed and extracted together with the piece of cotton wool. The yield from this was 5,000 M.U. Further experiments were carried out in the following manner: the animals were killed at different intervals after the injection of estrone and estrone benzoate. The oil under the skin at the site of injection, together with a piece of the surrounding tissue, was extracted apart from the remainder, according to Method 2a. The results are listed in Table II.

It is evident that six hours after the injection of free estrone, an average of 10 to 25 per cent of the estrone was recovered from the site of injection; whereas, following the same lapse of time after the injection of the ester, 80 to 90 per cent was recovered. Twenty-four hours after the injection 50 per cent of the ester had not yet been absorbed. In one case, 15 per cent was still found under the skin forty-eight hours after the injection.

In the body itself, with the exception of one rat (No. 65, in which 6,000 M.U. were found), very small amounts of hormone or ester were discovered. We may assume that with this rat the site of injection had not been indicated correctly so that the greater part of the ester which had not been absorbed was extracted with the rest of the body. From

the experiments with estrone it appears clearly that, after six hours, no more than 25 per cent of the amounts injected was present at the original site of injection, while the remaining 75 per cent could not be detected in the animal organism.

TABLE II

NO.	ESTROGENIC HORMONE	QUANTITY OF E. H.		ANIMALS SACRIFICED AFTER: HR.	HORMONE FOUND		TOTAL AMOUNT OF HORMONE	
		UNITS	MG.		AT SITE OF INJECTION	IN THE FAT	UNITS	%
55	Estrone	10,000	1.0	6	2,500 (25%)	500	3,000	30
56	Estrone	10,000	1.0	6	2,500 (25%)	1,000	3,500	35
65	Estrone	40,000	4.0	6	500 (1%)	6,000	6,000	15
75	Estrone	20,000	2.0	6	2,000 (10%)	----	----	--
57	Estrone	1,000	0.1	24	100 (10%)	100	100	10
76	Estrone benzoate	5,000	2.0	6	4,500 (90%)	----	----	--
59	Estrone benzoate	1,000	0.4	6	800 (80%)	<200	±800	±80
60	Estrone benzoate	1,000	0.4	6	800 (80%)	<200	±800	±80
45	Estrone benzoate	1,000	0.4	24	500 (50%)	<100	500	50
53	Estrone benzoate	1,000	0.4	24	500 (50%)	<100	500	50
54	Estrone benzoate	1,000	0.4	24	800 (80%)	<100	800	80
49	Estrone benzoate	1,000	0.4	48	150 (15%)	100	----	--
56	Estradiol benzoate	1,000	0.125	48	100 (15%)	<100	----	--

The problem then arises, "What happens to the absorbed estrone?" In the first place the possibility of conversion of the estrone after absorption into an esterified form (which has one-fourth of the physiologic potency of the estrone) had to be excluded. If we assume an esterification two possibilities arise. There could have been formed a lipid soluble ester or a lipid insoluble one similar to the form excreted in human urine. The latter possibility could be excluded since with our different methods of extraction (neutral as well as acid) the same values had been obtained, which results could be confirmed in control experiments. The problem was elucidated in the following way (Table III). As usual the rat was extracted in neutral medium, the free hormone as well as its lipid soluble ester, if formed, passing into the benzene phase. Now the mash was strongly acidified and extracted under reflux with benzene for four hours. In this manner any lipid insoluble ester present is hydrolyzed. The hormone, thus liberated, would be readily recovered by the subsequent benzene extraction. In order to prove a possible formation of lipid soluble ester, a part of the residue obtained

TABLE III. THE ANIMALS WERE KILLED SIX HOURS AFTER INJECTION

NO.	INJECTION ESTRONE	FOUND UNDER SKIN		AFTER NEUTRAL EXTRACTION OF RAT		AFTER ACID EXTRACTION OF RAT
		BEFORE HYDROLYSIS	AFTER HYDROLYSIS	BEFORE HYDROLYSIS	AFTER HYDROLYSIS	
7	10,000 M.U. lmg.	----	----	1,000	1,000 U	
9	10,000 M.U. lmg.	1,000	1,000	500	500	<50 M.U.
10	10,000 M.U. lmg.	2,000	2,000	500	500	<50 M.U.
11	10,000 M.U. lmg.	1,000	1,000	200	200	100 M.U.

from the neutral extract was refluxed for four hours with alcoholic potassium hydroxide. The bulk of the alcohol was evaporated and the residue dissolved in water, acidified and extracted with benzene. The free estrone should be found in the latter. No increase of the estrogenic activity after hydrolysis could be found in the skin or in the mash. The same proved true after acid hydrolysis of the mash which had been previously extracted in neutral medium.

One more possibility still remained to be investigated, viz.: whether the hormone injected circulates through the body in the form of its hydrate. In order to detect this compound, the potency of the extract in regard to its capacity to cause opening of the vagina was determined in infantile rats. The method of doing this has already been described in connection with the urine studies. Judging from the amount of estrogenic units necessary to cause opening of the vagina it appears that the estrogenic substance was not estriol. These results confirm the observations of Zondek.

As regards the possible fate of injected benzoates of estrone and estradiol, the following possibilities must be considered: (1) The benzoate is hydrolyzed by enzyme action liberating estrone. (2) The benzoate is absorbed and is circulating as such through the body. (3) The ester is hydrolyzed elsewhere in the body, the freed hormone then exerting its action. (4) The freed hormone is converted again into an ester in the body but into a lipid insoluble one.

All these possibilities have been investigated.

1. Two rats (Nos. 70 and 71) receiving 10,000 mouse units (4 mg.) and two rats (Nos. 87 and 88) receiving 5,000 mouse units (2 mg.) of estrone benzoate were killed six hours after the injection. The oil together with the surrounding tissue was removed in the usual manner. After neutral extraction the benzene extract was assayed for its estrogenic activity. In Rats 70 and 71, 7,500 and 7,000, while in Rats 87 and 88, 3,750 and 3,000 units, respectively, could be found at the site of injection, unabsorbed. Parts of these four neutral extracts, equivalent to 1,000 estrogenic units, were evaporated, the residues dissolved in 50 c.c. of 50 per cent alcohol and boiled under reflux for four hours (after adding potassium hydroxide). The bulk of the alcohol was evaporated, the residues were diluted with water and acidified with hydrochloric acid to Congo red. The acid solution was shaken four times with benzene. The estrogenic activity of the benzene extracts was then assayed. After hydrolysis, 3,000 and 3,500 mouse units, respectively, were found in the four extracts. (As is known, the international unit of estrone is 0.1 gamma. In this laboratory the equivalent amount of estrone benzoate is found to be 0.4 gamma.) Accordingly, after hydrolysis of 1,000 estrogenic units (0.4 mg.) of estrone benzoate, we obtain theoretically 4,000 mouse units of estrone. In the above experiments we found an increase of the action from 1,000 to 3,000 and 3,500 mouse units. In other experiments we found a fourfold increase in potency. From these results we may conclude with certainty that the part that had not been absorbed still consists of unaltered benzoate.

2. After removing the parts containing the nonabsorbed hormone^{*}, the bodies of the rats (Nos. 70, 71, 87, 88) were minced and after drying with anhydrous sodium

sulphate were extracted with benzene, according to Method 3. In the extracts of Rats 70 and 71, 1,500 and 2,500, and in those of Rats 87 and 88, 600 and 1,200 mouse units, respectively, were found. Parts of these rat extracts, equivalent to 1,000 estrogenic units, were boiled with reflux with alcoholic potassium hydroxide for two hours. From the alkaline solution, benzene extracts were obtained in the manner already described. After this alkaline hydrolysis, 800 to 1,000 mouse units could be recovered. This indicated that the substance circulating through the body after the injection of estrone benzoate is no longer this ester but probably, for the greater part, free estrone.

3 and 4. Finally it was shown that after the injection of estrone benzoate no increase in the amounts of lipid insoluble estrogenic hormones are formed in the organism. Therefore, the minced specimens of lipoids after neutral extraction were boiled in strong acid solution for four hours. (It is known that the bound hormone occurring in urine is hydrolyzed in acid medium.) The acid mixtures were extracted with benzene for three periods of four hours each, the benzene being renewed each time. The combined benzene extracts were assayed. After this hydrolysis in the mixed specimens of Rats 70, 71, and 87, less than 100 mouse units of estrogenic substance could be found. The acid benzol extract of Rat 88, however, contained 200 mouse units. After neutralization each mass was boiled with alcoholic potassium hydroxide for four hours, all the proteins being thus hydrolyzed. The extracts were worked up as usual and in all cases proved to contain less than 50 units. The results are summarized in Table IV.

TABLE IV

NO.	QUANTITY OF ESTRONE- MONOBENZOATE		KILLED AFTER HOURS	UNITS FOUND UNDER THE SKIN		IN THE RAT AFTER NEUTRAL		ACID EX- TRACT
	UNITS	MG. SUB- STANCE		BEFORE	AFTER HYDROLYSIS	BEFORE	AFTER HYDROLYSIS	
70	10,000	4	6	7,500	$3 \times 7,500$	1,500	1,500	100
71	10,000	4	6	7,000	$3.5 \times 7,000$	2,500	2,500	100
87	5,000	2	6	3,750	$3.2 \times 3,750$	600	± 600	100
88	5,000	2	6	3,000	$4 \times 3,000$	1,200	$\pm 1,200$	200
82	2,500	1	48	100	3.5×100	65	± 65	50
83	2,500	1	48	150	4×150	100	± 100	50
84	2,500	1	48	200	3.5×200	65	65	50

In the body neither lipid soluble nor lipid insoluble esters were found. In the former case, an enhanced estrogenic reaction was to be found after saponification of the neutral extract from the mash; in the latter case free hormone must have been detected in the acid extract which was obtained after the neutral extraction of the mass. A protracted action of the benzoate ester is certainly not caused by a slow cleavage of the acid component in the body.

The longer period of estrogenic effect noted after the injection of the benzoate ester into ovariectomized mice is due to its delayed resorption.

Where in the body the estrogenic substances are inactivated still remains an open question. According to Zondek, mashed liver could inactivate estrone *in vitro*. Our preliminary experiments did not confirm this assumption; further investigations are to be continued.

SUMMARY

1. After administering large amounts (2.5 mg.) of estrone to rats only very small quantities were recovered in the urine and feces which were collected for eight days after the injection. For this reason the hormone content of the whole animal was investigated.

2. During this investigation three different extraction methods were used and gave the same results.

3. After injecting estrone and estradiol a small part only was recovered from the animal body six hours afterward.

4. Six hours after administering estrone benzoate the bulk of it could be recovered unaltered, while often 50 per cent of the estrogenic units had not yet been absorbed as long as twenty-four to forty-eight hours after the injection.

5. After the injection of the benzoate ester this substance does not circulate through the body as such but as free hormone.

6. The protracted action of the benzoate is due to its delayed absorption and not to the slow hydrolysis of the ester in the body.

7. After administering estrone or estradiol, lipid insoluble estrogenic hormones similar to those occurring in the urine, could not be found.

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THE STANDARDIZATION OF ANTERIOR PITUITARY HORMONES

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SINCE Evans¹ first showed that anterior pituitary extracts could influence growth, many reports of studies upon the physiologic effects of the implantation of anterior pituitary substance or of the injection of various extracts of the fresh or preserved glands have appeared. In fact, in recent years the number of papers dealing in one way or another with this important subject has been growing almost by geometric progression. A critical analysis of these various contributions shows beyond any doubt that many clear-cut and distinct physiologic effects can be produced by anterior pituitary extracts. The question has arisen repeatedly in the mind of the individual worker as to whether the apparent specific effect of a certain extract is due to a specific anterior lobe hormone or active principle or to an active principle which has in addition other physiologic activities. Since the actual properties of anterior lobe extracts are so many and so varied, it becomes on a priori reasoning a matter of grave doubt that the number of active principles can equal the number of known specific effects. The writer has long since come to the conclusion that irrespective of the number of physiologic effects which may be demonstrated for various anterior lobe preparations, and irrespective of the apparent purity in a physiologic sense of this or that extract, the number of active principles in the normal gland in the living subject must of necessity be few (three or four). I do not believe that anyone has as yet obtained an anterior lobe extract without some modification of the active principle or principles present in the living gland having taken place. Although I have no very strong evidence for it, I like to visualize the naturally occurring anterior lobe hormone or hormones as rather large protein molecules to each of certain prosthetic groups of which some specific physiologic effect may be related. Such a view allows at least of one cherishing the hope that some day simpler compounds having specific physiologic effects may be obtained in crystalline form. These would not be true hormones but breakdown products resulting from controlled hydrolytic or other processes yet to be discovered.

Meanwhile, even though the number of effects of anterior pituitary extracts is still increasing, it becomes most essential that some system of biologic standardization of extracts should be agreed upon, particularly

so that experimental clinical studies can be satisfactorily made and the results of such adequately evaluated. At the present time, there is not enough information to allow of the setting up of absolutely rigid standards, but an attempt can be made in this direction, and in the course of time, as more exact knowledge becomes available, methods of testing which are universally acceptable may be agreed upon.

DISCUSSION OF ASSAY METHODS

GROWTH

Exact assay of the growth principle is a matter of great difficulty for various reasons. Probably the best test object is the recently hypophysectomized rat weighing about 100 gm. The minimum amount of extract given twice daily by subcutaneous injection which will result in an average gain in weight of 1 gm. per day over a period of ten to fifteen days may be taken as a unit. Normal rats whose growth curves have tended to plateau may be used also according either to the method of Evans and Simpson² or Lee and Schaffer.³

Even though by the use of a sufficiently large number of animals an apparently satisfactory assay has been made on any one particular extract, there still remains the possibility that the growth principle present may have been enhanced or inhibited by the presence of other substances in the extract under test. Difficulties such as these are bound to be encountered not only in the assay of the growth principle but also of other principles until such time as the individual active substances are obtained in relatively pure form. In a growth extract made by the "Q" process there is probably a minimum of other active principles.⁴ This extract is impractical, however, since the yield of active substance may be as low as 5 per cent. On the other hand, a simple alkaline extract containing small amounts of practically everything in the original gland tissue may cause a positive growth response in the hypophysectomized rat when the equivalent of as little as $\frac{1}{2000}$ gm. of pituitary is given per day. Again certain extracts rich in thyreotropic hormone may appear to have little or no growth effect when tested on hypophysectomized rats but a "Q" fraction may be obtained from such a mixture by the use of $\text{Ca}_3(\text{PO}_4)_2$ which can be shown to have considerable growth-promoting power.

THE THYREOTROPIC PRINCIPLE

The thyroid-stimulating principle of anterior lobe extracts can be assayed according to one or other of various criteria with a fair degree of accuracy, but here again, as in the case of the growth hormone, one cannot be sure in dealing with any one extract containing this substance whether the assay value obtained represents an increase or a

decrease over the exact value due to the synergistic or inhibitory action of associated substances. There are several fairly exact methods for measuring the potency of an unknown extract to influence the thyroid gland. Unfortunately, however, the results obtained by one method, even though they may be readily duplicable, may not parallel the results obtained by a different method. Observations of this kind, while at the moment very confusing, point very strongly, as Heyl and Laqueur,⁵ and Collip⁶ have suggested, to the possibility that the anterior pituitary may influence the thyroid gland in more than one way. The methods of assay which have been suggested for the thyroid stimulator may be classified as follows:

1. Those depending upon the increase in the thyroid weight following treatment according to a definite schedule.
2. Those depending upon change in histologic structure.
3. Those depending upon changes produced in metabolism.
4. A method depending upon changes in the iodine content of the thyroid gland.

THE INDIVIDUAL METHODS OF ASSAY

1. Rowlands and Parkes⁷ make use of the percentage increase in the weight of the thyroids of guinea pigs weighing 200 gm. The extract to be assayed is injected daily for six days. Controls consist of untreated animals and animals treated with a standard extract. The unit is taken as the amount which causes a 50 per cent increase in the thyroid weight during the time of the test. It is essential for accurate work that the pigs should be raised under well-controlled conditions of housing, feeding, temperature, etc.

Riddles⁸ has found that the young dove or pigeon may be used to advantage for thyreotropic hormone assay, but as yet there has been no attempt to correlate the bird and the guinea pig unit.

2. The production of hyperplasia as demonstrated histologically or cytologic changes associated with hyperfunction has been a favorite method with various workers (Junkmann and Schoeller,⁹ L. Loeb and Friedman,¹⁰ Krogh and Okkels,¹¹ etc.).

The histologic method recently described by Heyl and Laqueur⁵ is in our opinion the most accurate as well as serviceable of this type: 200 gm. guinea pigs are injected intraperitoneally on each of two days and killed at forty-eight hours. The detection by histologic study of the first delicate changes which occur in the acinar cells is made the basis for a positive reaction.

The restoration to normal of the atrophic thyroid gland of the hypophysectomized rat can be used as an alternative method of assay in this group, dependent upon structural change demonstrable by microscopic examination. When this method is made use of, the animals should be of a certain age group and used at a definite time after hypophysectomy.*

3. The increase in metabolism of the hypophysectomized rat operated upon at a definite age and otherwise untreated gives a very satisfactory criterion for assay of the factor in anterior lobe extracts responsible for the elevation in metabolic rate.

*Another method which has much to commend it has been reported by Starr and Rawson at the Atlantic City meeting of the American Society for Clinical Investigation, May 3, 1937. It is a micrometric analysis of the response of the guinea pig thyroid.

amenorrhea, secondary amenorrhea, and in a young castrated woman. What is understood by the term menstruation and what is understood as artificial menstruation must be borne in mind. We have to distinguish between two kinds of bleeding: (1) Bleedings from proliferated uterine mucosa, and (2) hemorrhage from a mucosa in the progestive phase. The studies of American authors on the induction of uterine bleedings in monkeys may have brought about a little confusion. In the summer cycle of the female monkey there exists a periodical non-ovulating bleeding from proliferated mucous membranes. (Hartmann et al.) Similar cyclic hemorrhages also occur in the human female. In the latter instance the ovaries produce the follicular hormone only, but not the corpus luteum hormone. This bleeding must be classed as pseudomenstruation. Only the hemorrhage from a secreting mucous membrane, i.e., from a uterine mucous membrane on which the corpus luteum hormone (progesteron) has exerted its influence, can be called true menstruation. It is solely in a mucous membrane of this type that a fertilized egg can develop. As is well known, menstrual blood differs from ordinary blood by its inability to coagulate. If bleeding is induced in a castrated woman by follicular hormone (200,000 to 300,000 M. U.), this blood likewise does not coagulate according to my observations. This means that blood shows the same characteristics in pseudomenstruation as in true menstruation. On the other hand, the hormonal mechanism is very different in pseudomenstruation and menstruation. Therefore you cannot explain the mechanism of menstruation in a human female through data obtained on pseudomenstruation in monkeys.

In a castrated woman, it is sufficient to induce hemorrhage by administering follicular hormone, i.e., to produce a pseudomenstruation. With the beginning of the bleeding, the woman will lose her subjective complaints and she will see in the returning of the bleeding an expression of her regained female functions. However, in a case of amenorrhea in the procreative age, one should not be satisfied by producing pseudomenstruation only; moreover, folliculation and real menstruation should be induced in order to make conception possible. However, this result cannot be obtained by ovarian, but by gonadotropic hormones only. In such an instance therapy by hormonal substitution will not be sufficient, but we will need hormonotropic stimulation.

In the present studies I artificially induced uterine bleedings in amenorrheic women and in one castrated woman, and then analyzed the urine for prolan A.

To prove the presence of small amounts of prolan A, I formerly used the method of precipitation by alcohol.² Later on, together with Scheibler and Krabbe,³ I demonstrated the method of precipitation by phosphotungstic acid and phosphomolybdic acid, respectively. Katzmann and Doisy⁴ use a similar method: precipitation by tung-

seventy-two hours.* The rats used for assay are twenty-one days old at the beginning of the test. In order to bring the clinical unit for this substance more in line with the placental hormone of pregnancy blood and urine (A. P. L.), I suggest that the clinical unit be one-tenth of that defined above. Many variations of the immature rat test have been used and reported from different laboratories. Thus injections may be made once, twice, or three times daily; vaginal smears can be taken and if one wishes can be made the criterion of activity. One point of extreme importance, irrespective of which modification of the rat test is being used, is that the injections be made subcutaneously. Intraperitoneal injections are absolutely useless if an accurate assay is to be made.

ADRENOTROPIC SUBSTANCE

The adrenotropic substance in our experience cannot be satisfactorily assayed on other than an hypophysectomized animal, preferably the rat. The restoration toward normal of the atrophic cortex of the hypophysectomized rat is at present the method of choice for the determination of adrenotropic potency. Large doses of adrenotropic extracts may produce enlargement of the suprarenal cortex of the normal rat but since so many nonspecific agents have been shown to produce a similar result (probably through the release of adrenotropic substance from the intact pituitary) I consider it absolutely unsafe at this time to use the normal animal for this purpose. Unfortunately, no test based on a physiologic response has been discovered as yet. The technic of carrying out the test as originally described is as follows:

The left adrenal is removed from hypophysectomized rats ten days to two weeks following the operation. This gland is weighed and sectioned for microscopic examination. The animal is injected twice daily for six days with the extract to be tested. The animal is killed and the right adrenal is weighed and sectioned, as is also the thyroid gland. Control experiments have shown that there is no compensatory hypertrophy of the remaining gland after unilateral adrenalectomy in the hypophysectomized animal. Increase in weight of the remaining adrenal over that of the one taken at biopsy, together with microscopic evidence of cortical repair, is taken as positive evidence of adrenotropic activity in the extract. The minimum amount of extract given daily which caused a 50 per cent increase in the weight of the gland was taken as the unit.

A modification of this test consists in using a larger number of hypophysectomized animals and eliminating the removal of one gland. Since it may be assumed that the weight of the glands in untreated

*A new method for the assay of follicle-stimulating substances has been reported recently (Annual meeting of the Federation of Biological Societies, Memphis, Tenn., April 22, 1937) by Levin and Tyndale. The effect of graded doses of a gonadotropic extract upon uterine weight of the mouse is used as the basis for assay.

We have suggested as a unit, using this method, the minimum amount which when injected subcutaneously twice daily for three days causes an increase in metabolism of 20 to 25 per cent.

Because this method presents many difficulties, we have been attempting to correlate with it a similar procedure in which normal guinea pigs weighing 200 gm. are used. We are endeavoring as well to correlate histologic change and thyroid weight increase both in hypophysectomized rats and in normal pigs with the metabolic response of each. It is too early to draw final conclusions from this work, but it is our impression that ultimately assays will have to be made both for the metabolic effect and for the thyroid enlarging effect since we have noted on several occasions marked differences in regard to these two effects in the same extract. These observations suggest that the enlargement of the gland and the release of thyroid hormone are two separate and distinct functions. If this proves to be true, then the problem of clinical goiter in relation to the anterior pituitary will tend to become less obscure.

4. McCulloch and Stimmel¹² have suggested as an alternative method of assay for the thyreotropic principle the decrease in the iodine content of the gland of the treated animal. This method, which is only available to experts in iodine determination, should prove of great value in the solution of the problem suggested in the previous paragraph.

THE GONADOTROPIC PRINCIPLE

There are numerous methods of demonstrating the maturity or gonadotropic activity of anterior pituitary substance or extracts. Thus either males or females of widely divergent species may be used. From my own experience I prefer to use the immature female rat. The immature male, the prepubertal or postpubertal hypophysectomized male or female rat, may also be used. The immature male dove or pigeon has been shown by Riddle^{8, 13} to be an excellent test object for follicle-stimulating hormone. Many others use the ovulation test in the estrous doe. Laboratory studies generally with the gonadotropic substance are complicated by the fact that there probably are two factors involved at least in the case of the female, one the so-called follicle-stimulating hormone (F. S. H.) and the other the luteinizer or L. H. A full discussion of this topic is not indicated here; suffice it to say that in view of the apparent synergistic action between these, it is practically impossible in the light of the work of Fevold and Hisaw¹⁴ to obtain an absolute value for the F. S. H. content unless the extract being tested is free of L. H.

The usual effect of treatment by subcutaneous injection of immature female rats with a good preparation of gonadotropic substance is a rapid increase in ovarian size, which reaches a maximum in from seventy-two to ninety-six hours. Since the upper limit of ovarian weight does not as a rule exceed 60 mg., irrespective of the size of the dose administered, I have suggested as a laboratory unit of gonadotropic potency the minimum amount which, injected daily in three divided doses for three days, produces ovaries of 30 to 40 gm. in weight in

and is apparently independent of the thyreotropic hormone. This type of metabolic response is best studied upon thyroidectomized animals.

Some other effects of anterior lobe extracts, such as those upon liver size and fat content, protein metabolism, skeletal form and architecture, and blood calcium and calcium metabolism are known and methods for study of all of these are available; but it is doubtful to my mind whether any of this group of reactions will be of practical value in relation to the standardization of anterior lobe extracts for clinical use.

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animals will be from 9 to 12 mg., a dose of extract is found which will cause the glands to increase approximately 50 per cent in weight in a period of five days.

PROLACTIN

That substance present in certain anterior lobe extracts which appears to be purely a secretagogue to the fully developed mammary gland and which has been so extensively investigated by Riddle and his coworkers,¹³ also by Gardner and Turner,¹⁵ and others, is assayed by choice by the crop gland response of the immature dove or pigeon. This method was introduced by Riddle and has been standardized perhaps to a more satisfactory degree than is the case with most hormone assay methods. The unit, as it has been defined by Riddle, was based on the crop gland response in the two-month-old squab, comparison being made of the unknown with a standard preparation, 1 mg. of which was the threshold dose per 150 gm. of pigeon. Injections were made intraperitoneally daily for four days. It is of interest in connection with prolactin that the crop gland response has been shown by Riddle to vary tremendously depending upon the mode of administration of the extract. Subcutaneous administration is many times [as high as 20] as effective as intraperitoneal injection. My own experience with prolactin has been similar to that of Riddle. It is very important, therefore, in the assay of this anterior pituitary hormone, as in the case of the gonadotropic factor, that the site of injection be carefully controlled.

Lyons and Page¹⁶ have shown that a local crop gland response can be induced by the intradermal injection of a very minute amount of an active extract over the site of the crop. This is the most sensitive test known for the hormone and is of great value for detecting the presence of prolactin. For the present, however, Riddle's method appears to me to be the most reliable for accurate biologic assay of extracts designed for human use.

There are other physiologic effects of anterior lobe extracts for each of which there are methods of testing. These methods allow of an approximate determination of the potency of the extract in regard to each of a variety of effects. Thus the so-called diabetogenic action of anterior lobe extracts can be examined by noting the effect upon blood and urine sugar and acetone bodies of standardized Houssay dogs which have been treated with the extract.¹⁷ The ketogenic action of extracts can be studied independently of the blood sugar raising action by using the young normal fasted rat.¹⁸⁻²¹

Recently, O'Donovan, working in my laboratory, has shown that the injection of certain pituitary extracts may cause a sharp rise in the metabolic rate which, however, is very transitory, lasting for only a few hours. This effect has been obtained in thyroidectomized animals

was 100.6°; there was precordial pain and palpitation on exertion. At first it was thought these symptoms might be due to rheumatic fever, but it was soon evident that they were due to widespread metastases in the lungs, the bony structure, and probably also the valves and muscle of the heart. She was readmitted to the



A.



B.

Fig. 1.—A, Liposarcoma of the left labium majus. B, Operative specimen removed in continuity with the superficial inguinal and femoral lymphatics.

hospital January 20. The urine contained bacilli, considerable pus, albumin, and casts. An x-ray picture (Fig. 2) taken January 27 showed: "rib structures, lumbar spines and bones of the pelvis, including heads of both femurs, indicate unmistakable evidence of metastatic changes characterized by bone rarefaction. The lungs present

SARCOMA OF THE VULVA

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SCARCELY less thrilling than the discovery of some rare flower by the botanist or a new star by the astronomer is the detection of an unusual form of tumor by those interested in pathology. Furthermore, it is through the careful analysis of the unusual that we sometimes find an answer to our everyday problems. Hence, it was with some satisfaction that in the past year I chanced upon the two unusual examples of sarcoma of the vulva that comprise this report. These two cases included a liposarcoma of the labium majus and a lymphosarcoma of the clitoris.

The best summary of our present knowledge of sarcoma of the vulva is to be found in the chapter contributed by E. Kehrer³ to the *Veit-Stoeckel Handbuch*. Excluding, as seems to me quite proper, all cases of so-called melanosarcoma, he finds record of 77 cases of sarcoma developing from some portion of the external genitals. Anatomically data were available in 70 instances and these showed the following distribution: right labium majus, 23 cases (33 per cent); left labium majus, 20 cases (28.5 per cent); clitoris, 8 cases (11.4 per cent); labia minora, 3 cases (4.3 per cent); periurethral, 8 cases (11.4 per cent), and various combined lesions, 8 cases (11.4 per cent). In a small group comprising 14 cases collected by Nebesky⁸ the sarcoma started in the urethra itself and extended to the vulva and vagina secondarily. B. P. Watson¹² also reports a case of this kind.

CASE REPORTS

1. *Liposarcoma of the Labium Majus*—

H. H., twenty-nine years of age, married, para i, came to the Barnard Free Skin and Cancer Hospital Aug. 11, 1936. She had no family history of malignant disease and had always been in good health, until the present illness. Four years previously at the age of twenty-five she had noticed a small hard lump in the left labium majus. This lump had suddenly grown larger in the past six months, and six weeks previous to coming to our hospital the tumor had been enucleated by another surgeon under the diagnosis of fibroma. Subsequent pathologic diagnosis of this specimen, concurred in by Leo Loeb, was liposarcoma. Two weeks after removal the tumor had recurred and on admission was 4 by 2½ cm. in size, adherent to the skin but freely movable over the underlying fat of the vulva and without ulceration (Fig. 1). In the left inguinal region a hard gland 1½ cm. in diameter could be felt. The patient was in excellent physical condition, had not lost in weight, and showed no evidence of metastasis at this time. In view of the well-known difference in method of metastasis, it was decided to abstain from the type of complete vulvectomy with extensive lymph gland resection (Basset operation) recommended for carcinoma of the vulva. Instead of this we did a one-sided vulvectomy removing merely the left-sided superficial inguinal and femoral lymph glands in continuity with the tumor. This operation was done Aug. 15, 1936 and the wound was completely healed five weeks later. Two months after this the patient began to have left lumbar backache and pains in the hips, spines, and shoulders. She was confined to bed at home. On Jan. 5, 1937 the temperature

lesions that are probably associated with metastasis." A blood transfusion of 500 c.c. given January 30 on account of progressive anemia availed but little. Pneumonia developed and death ensued Feb. 7, 1937. Autopsy was refused.

Pathologic report (Dr. Louis H. Jorstad): "Specimen is one-half of the vulva. At midpoint is a tumor pushing up the skin and on section this is a mass measuring

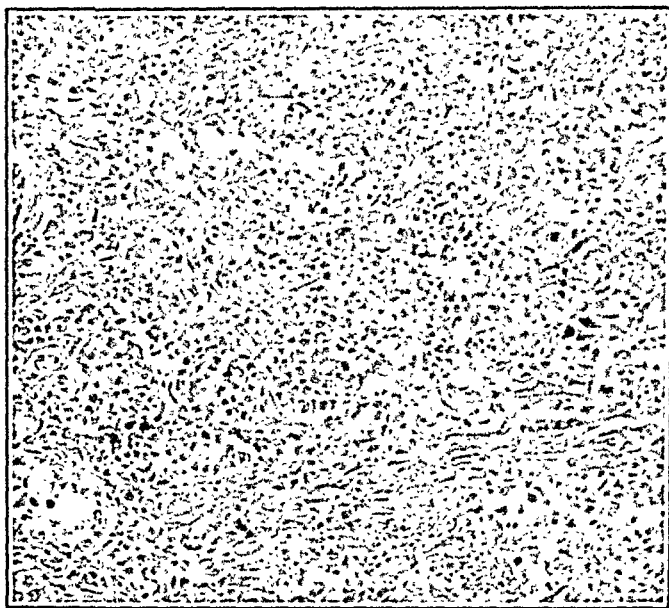


Fig. 4.—Section of liposarcoma, stained with hematoxylin and eosin. Magnified 90X.

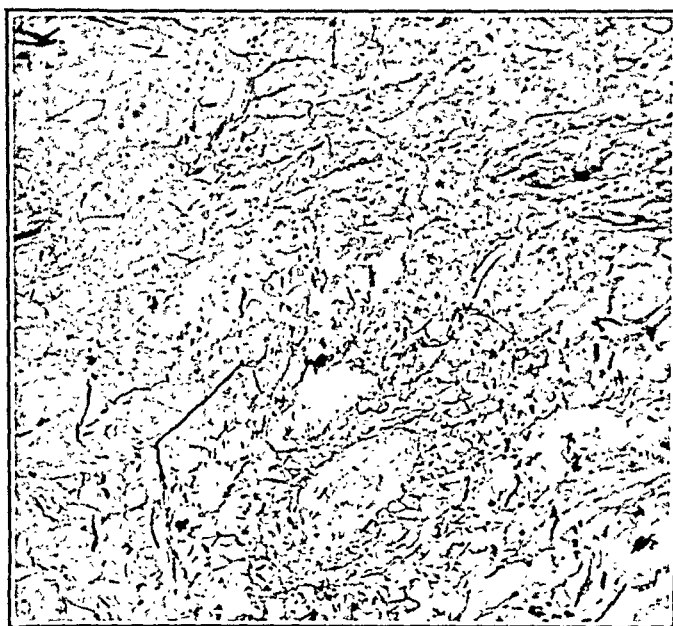


Fig. 5.—Section of liposarcoma, stained by the Foot-Bielschowsky silver impregnation method for reticulum fibers. Magnified 200X.

3½ by 2½ cm., situated in the vulvar fat, not attached to the skin (Fig. 3), for the most part opaque in color, with areas, however, of fatty color. It has somewhat of an alveolar arrangement. Along with the vulva is a mass of fatty tissue containing a number of lymph nodes. These are not particularly increased in size, are soft and quite normal in color."



Fig. 2.—Roentgenogram of bone metastasis following liposarcoma of the vulva. Note especially the frayed-out lateral edge of the left ilium.



Fig. 3.—Low-power microphotograph of liposarcoma, showing definite fibrous capsule and separation from the skin (hair follicles visible).

gland involvement. In both groins there were numerous enlarged lymph glands and one hard femoral gland on the right side seemed definitely the seat of a metastasis. The clinical diagnosis of cancer of the clitoris was made. It was decided to do a vulvectomy and, if conditions permitted, to follow this two weeks later by a Basset removal of the tributary lymph glands.

On Sept. 28, 1936 at the Jewish Hospital the entire vulva was removed under local anesthesia. The patient made a satisfactory recovery from this operation. When the report came back that the tumor was a lymphosarcoma, it was thought wiser in view of this fact and the poor physical condition of the patient to be content with a simple superficial removal of the evidently enlarged glands on both sides. This was done Oct. 12, 1936. With the exception of the usual partial sloughing of



Fig. 6.—Lymphosarcoma of the clitoris, involving the prepuce and right labia with perforation ulcers.

the inguinal wounds the patient seemed on the way to recovery and was allowed to be out of bed for a short time after the twelfth day. On October 27, fifteen days after the second operation, while seated in the wheel chair, she suddenly collapsed, became cyanotic and died in thirty minutes, evidently as a result of embolism. Autopsy was refused.

Pathologic report (Dr. Sam Gray). *Microscopic:* Specimen consists of an excised vulva measuring 9 by 13 by 3 cm. The clitoris consists of a firm, rounded, red mass measuring 2 by 1½ cm. The frenulum and prepuce are well defined, the latter being quite edematous and containing two small, firm nodules, one of which is reddened and ulcerated. Just above the clitoris is a round, firm mass 3 cm. in diameter, presenting an ulcerated punched-out area in the center. Just above this nodule, deep in the subcutaneous tissues, is another firm area which, on cut surface, is irregular, white and firm. The right labium minus is indurated and discolored

Microscopic diagnosis: Liposarcoma with hyperplasia of lymph nodes. Sections sent to Dr. James Ewing confirmed this diagnosis.

"Sections of the tumor stained with hematoxylin and eosin show a moderately rich cellular neoplasm separated into smaller and larger masses of fine and coarse bands of fibrous tissue (Fig. 4). The tumor cells are oval to spindle in shape, vary markedly in size, the nucleus is small, and the cytoplasmic structure contains fat globules of varying size and number. The cytoplasm is finely granular. These cells represent varying stages in the development of fat cells. The reticulum of the tumor demonstrated by the Foot modification of the Bielschowsky silver impregnation method is abundant in quantity and mainly in the form of a plexus surrounding each cell, the whole forming a network (Fig. 5). The intracellular fat was demonstrable in the frozen section, stained with Sudan III. The lymph nodes present a moderate hyperplasia, with no evidence of tumor cells."

DISCUSSION

Liposarcoma has been found in the uterus, the mammary gland, the kidney, bones and extremities. Kehrer³ describes large and small round cell sarcoma, fibrosarcoma, myxosarcoma, and fibromyxosarcoma of the vulva. Only one case reported by Kleeberg⁴ is described as a lipofibrosarcoma. According to Robert Frank² the histology of sarcoma of the vulva is varied, myxosarcoma, spindle-, and fibrosarcoma being most frequent. It seems not unlikely that with modern staining methods a few of these cases would have shown evidence of rising from the fatty tissue, especially in view of the predominance of tumors rising from the labia majora (61 per cent of the total). According to A. F. B. Shaw¹⁰ the characteristic features of liposarcoma are: (1) they occur in adult life of either sex; (2) they are slow growing for many years with sudden increase; (3) encapsulation, readily removable at operation, does not suggest malignancy; (4) local recurrence usual, often repeated; (5) death follows metastasis; and (6) varied histologic structure. This case followed closely the characteristic clinical course of these tumors.

2. *Lymphosarcoma of the Clitoris*—

B. B., sixty-three years, married, 9 children, consulted me September 25, 1936. Menopause at forty-five years, gradual, without symptoms. Patient said that eight months previously she had noticed two small lumps the size of a lima bean above the urethra. These lumps were not tender or painful and gradually increased to the size of a small lemon. For two months the tumor had become irritated and bled a little. No pruritus. Some burning after urination. Weight loss of 8 pounds in the past year. A small lump was noted by the patient in the right groin one week before consulting me.

Examination showed a rather feeble old woman with marked evidence of myocardial degeneration (intermittent, rather rapid, pulse), blood pressure 168/70, moderate emphysema and arteriosclerosis. Locally there was seen a hard nodular mass involving the entire clitoris and a portion of the right labium minus (Fig. 6). The tumor was evidently subepithelial in origin but at one point over the clitoris had penetrated through the skin with formation of an ulcer 1 cm. in diameter. The labial extension also showed an area of ulceration as seen in Fig. 7. The urethra on the other hand was entirely free of direct involvement, as were also the left labia. Internal exploration revealed normal pelvic organs and vagina, without palpable iliac

stic acid. However, the prolan values in the urine found by Katzmann and Doisy are lower than those I found by means of the alcohol precipitation method. Thus I cannot admit any superiority of the tungstic precipitation over the alcohol precipitation method. Precipitation by alcohol is simple and may be done easily in every laboratory.

In the following I wish to present in brief the cases under investigation:

SECONDARY AMENORRHEA

CASE 1.—M. Schw., twenty-eight years old, married five years, sterile. Menstruation started at fifteen years, almost regularly. Total amenorrhea for five years.

Urinalysis before treatment revealed at least 111 M. U. prolan A per liter morning urine.

From July 8 to 28, 1935, the patient received 10 injections of dimenformon^{*} (benzoate dihydrofollicularhormone). Every injection contained 50,000 M. U., i.e., a total of 500,000 M. U. of dimenformon.

The reaction of the morning urine from July 29, at the end of the treatment with dimenformon, was negative and the 111 M. U. of prolan A per liter of urine was no longer demonstrable.

Nine days after stopping the dimenformon treatment, a bleeding occurred, lasting four days. Urinalysis during menstruation was also negative.

Result.—In this case, increased elimination of prolan A was no longer noticeable after treatment with follicular hormone.

CASE 2.—Ch. E., thirty-six years old, married twenty-two years. The patient had been married at fourteen, before her first menstruation. She began menstruating at the age of fifteen and one-half years, regularly in the beginning, then at an interval of two to three months. For five and one-half years she has been amenorrheic.

Analysis of the urine before treatment was positive, i.e., there were at least 111 M. U. of prolan A per liter of morning urine demonstrable.

From June 23 to July 11, 1935, the patient received 14 injections of dimenformon, a total of 700,000 M. U.

During the treatment, i.e., after administration of 600,000 M. U. of dimenformon, the prolan reaction was negative, i.e., 111 M. U. of prolan were no longer demonstrable. The treatment was ineffective; there was no bleeding.

In July and August, 1935, the patient received 700,000 M. U. of dimenformon for a period of twenty days. After that she received 5 rabbit units of progesteron daily from the twentieth until the twenty-fifth day. After stopping the treatment, there was menstrual bleeding. Urinalysis was again negative.

Result.—It was not possible to induce pseudomenstruation by administration of follicular hormone, but excessive elimination of prolan A was abolished. By a combined treatment with follicular and corpus luteum hormone, menstruation could be induced and simultaneously increased excretion of prolan A was abolished.

PRIMARY AMENORRHEA

CASE 3.—Ch. A., thirty years old, married thirteen years. She never menstruated. The uterus was hypoplastic, 4 cm. long.

On May 8, 1935, before the treatment began, the urinalysis was positive. There were at least 111 M. U. of prolan A per liter of morning urine demonstrable. With-

^{*}I am indebted to the "Organon" factory (Oss, Holland) for supply of dimenformon.

and has an ulcerated area with a firm base, $1\frac{1}{2}$ cm. in diameter. No other areas of induration are found in the specimen, the undersurface consisting of fat and subcutaneous tissue.

Microscopic: The section is that of the clitoris, the surface of which presents intact normal epithelium (Fig. 8). Just beneath the epithelium there is a dense aggregate of round cells, which are individual and show no syncytial arrangement. The majority of the cells are medium-sized lymphocytic structures with pale colored sparse cytoplasm. The nuclei are slightly irregular in outline, have a well-defined nuclear membrane and moderate amounts of chromatin loosely arranged in strands connecting irregularly shaped condensed masses. Nucleoli are frequently present and are irregular in outline. Occasional pyknosis of the nuclei is present. Mitotic figures are infrequent. Normal lymphocytes and plasma cells are rare. Typical



Fig. 7.—Same case as Fig. 6 with retractors in position to show that the tumor did not involve the urethra or vagina.

reticulum cells, with large vesicular nuclei containing fine strands of chromatin are occasionally encountered.

The morphology of the predominant cell type simulates the reticulum cell of the loose connective tissue more closely than the lymphocyte. Transitions between the two extremes can be found but the majority of the tumor cells show relatively slight differentiation from the more primitive reticulum (or mesenchymal) type of cell.

There is no evidence to suggest that this neoplasm is epithelial in origin. The epithelium is intact. The cells show no syncytial tendency. The slight amount of differentiation that is present is in the direction of a lymphocytic type of cell (Fig. 9). Diagnosis: Lymphosarcoma of clitoris.

Examination of the lymph glands removed at the secondary operation October twelfth showed merely normal hyperplasia with the exception of the large hard gland in the right femoral region which was filled with a metastasis showing the identical structure described in the primary tumor.

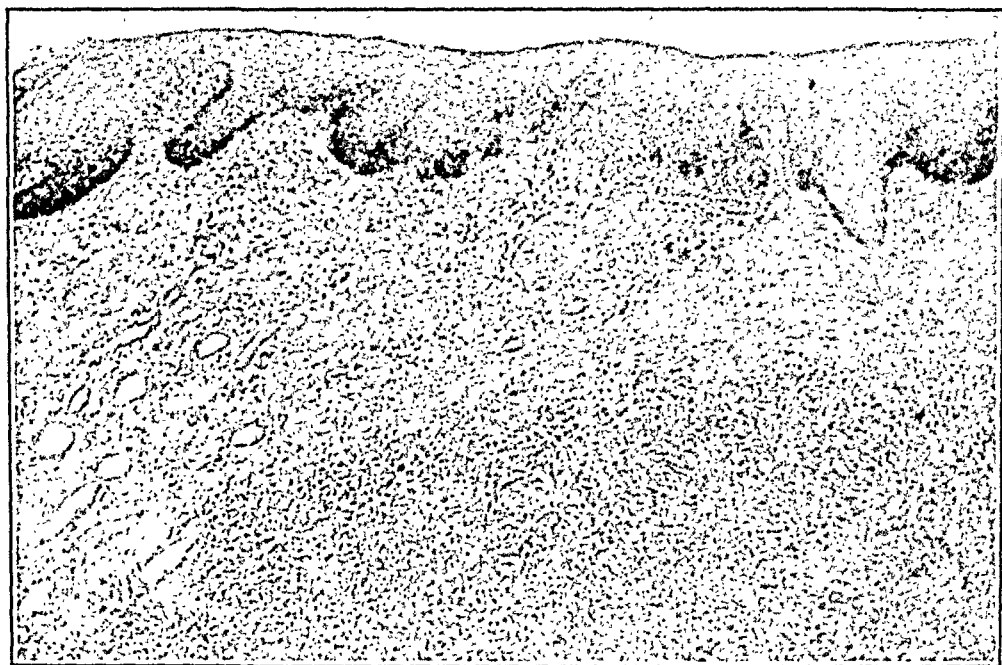


Fig. 8.—Section of lymphosarcoma of the clitoris, showing normal vulvar epithelium overlying the tumor. Magnified 110X.

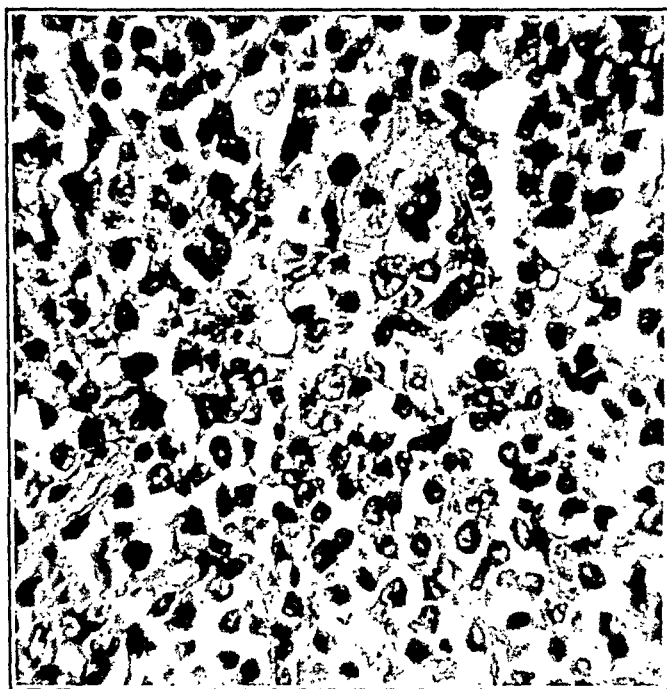


Fig. 9.—High power photomicrograph of lymphosarcoma of the clitoris, showing definite resemblance of the tumor cells to lymphocytes. Magnified 500X.

DISCUSSION

The designation of this tumor as a lymphosarcoma certainly seems justified in spite of the fact that it apparently represents the only tumor so classified to be found in medical literature. The changes that have recently taken place in the classification of malignant tumors may ac-

count for this, since doubtless many cases reported as round-celled sarcomas, if reviewed at the present time, would be classified as lympho-sarcoma. It is a striking fact that tumors springing from within the substance of the glans clitoridis (not those, however, that develop from



Fig. 10.—Anaplastic carcinoma of the glans clitoridis. Note the encapsulated sub-epithelial character of the tumor. Compare with Fig. 6.

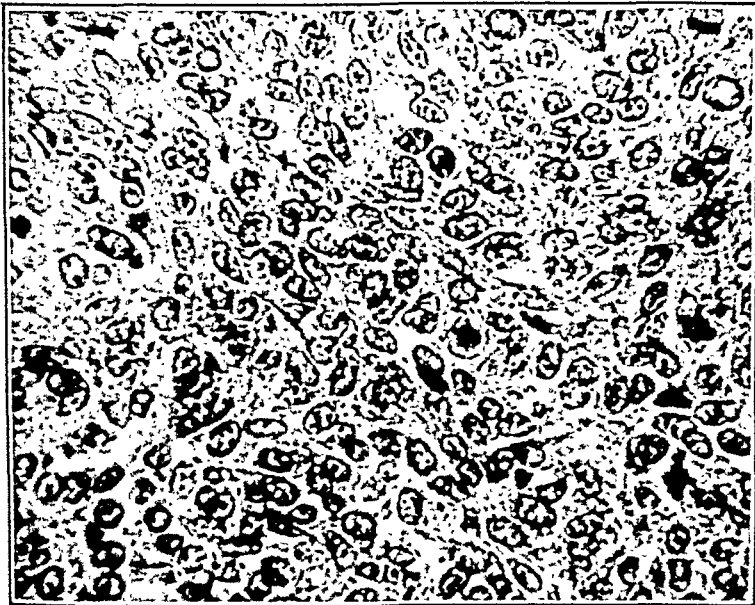


Fig. 11.—Section of anaplastic carcinoma of the clitoris, showing loose structure, many mitoses, but definite epithelial origin of cells. Magnified 500X.

the overlying preputial skin) have proved to be highly malignant. I¹¹ called attention to this fact some years ago in discussing carcinoma of the clitoris. Such tumors are often sarcoma-like, anaplastic in structure as seen in the section taken from a carcinoma of the clitoris (Figs. 10

and 11). It will be noted that the cells in this case have in areas a very loose structure with many mitotic figures. Nevertheless if this picture is compared with the microphotograph of the lymphosarcoma, the difference between the two cases will be apparent. It was only after a careful study that I became convinced that we were justified in grouping this case as a sarcoma rather than an anaplastic carcinoma.

CLINICAL ASPECTS OF SARCOMA OF THE VULVA

These two cases fit in closely with the clinical course of sarcoma of the vulva as previously described. Robert Frank² says: (p. 125) "They resemble fibromata until ulceration and infiltration takes place. . . . Early tendency to recurrence is the rule and multiple metastases may develop. The lymphatic glands are rarely affected, thus differing from carcinoma and melanoma." Frank Lynch⁵ considers the prognosis grave. Death appears to result uniformly in cases in which the diagnosis of vulvar sarcoma is firmly established. In five cases complicated by pregnancy E. Kehrer³ found that in none did the gestation seem to influence the growth of the tumor. In Maly's case the tumor was noted sixteen years before it suddenly grew larger and showed evidence of malignancy. In Blair Bell's¹ analysis of 18 cases of true sarcoma (not melanotic) of the vulva, the age distribution followed approximately that in cancer, the most frequent period being between thirty and fifty years. He found the myxomatous type of tumor the most common.

The diagnosis is usually made only after the disease is far advanced; hence, the treatment is usually very unsatisfactory. Surgery of the primary tumor is usually preferable to radiation and is ordinarily not attended by any difficulties. Only one case is on record where a five-year freedom from recurrence was reported (Maas-Olshausen).⁶ Even after five years there may be a recurrence (Rhomberg).⁹ The value of radium or deep x-ray therapy seems very questionable. Only a few cases have been treated by this method. All in all, sarcoma of the vulva presents at the present time a rather hopeless picture.

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THE TECHNIC OF TIMING HUMAN OVULATION BY PALPABLE CHANGES IN OVARY, TUBE, AND UTERUS*

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REASONING from a few cases studied intensively¹ and having happened upon occasional midinterval changes, I offer some tentative statements on the diagnosis of the time of ovulation and the organization of clinical research on this matter. Questions of methodology seem to be important because skepticism or failure of others in checking the findings may involve certain features that bear on confirmation. The first is one which only an Ancient can fully evaluate, namely, a degree of limitation in capacity for full visualization through the fingertips. This may be due to the lack of that training which we had in the early days of gynecology, that prelaparotomy elaboration of bimanual diagnosis forced upon us through absence of the safety of the open-look-see surgery of today, a later culture in which one has also had full opportunity. The second consideration is the careful choice of suitable subjects. The third is willingness to allow ample time for slowness of any given organ in its rhythm of contraction and relaxation, or for differing rates of travel of the wave of change through the various parts of a particular uterus. Herein the try-out of the Swedish pelvic massage of Thure Brandt taught us a special patience.²

For a *palpation research* on human ovulation the desirable factors seem to be the following:

- a. The subject should present minimal interference by adipose tissue in the lower abdominal wall and the omentum.
- b. The abdominal wall and pelvic floor should not be tense, as in athletic women.
- c. The intestinal tone should be good, so that little gas is in the bowel (and the bowel recently emptied).
- d. A varicosity of the broad ligament should be emptied by uplift of pelvis.
- e. The ovaries should be mobile and thus readily brought within reach; as is sometimes the case after a retroversion has been repositied and edemas have subsided, the ligaments being relaxed.
- f. The pelvic floor should yield freely to facilitate the reach up to the left ovary.
- g. The uterus would better be of the type given to well-marked rhythms of contraction and relaxation, and fully displaceable forward.
- h. That patient will be of most value who has some midinterval symptom such as breast ache, show, mucous discharge, well-defined pain or localized discomfort, especially if tenderness in one or the other lower abdominal segment can be elicited by deep pressure by her own fingertips. Also, in the case of distant residence, if she is one who will keep careful records.

*Read in part before Section on Gynecology and Obstetrics, New York Academy of Medicine, April 26, 1932. From the National Committee on Maternal Health, Inc.

The time of day best for the individual may be found to be after breakfast and recent bowel action, and of course immediately after bladder emptying.

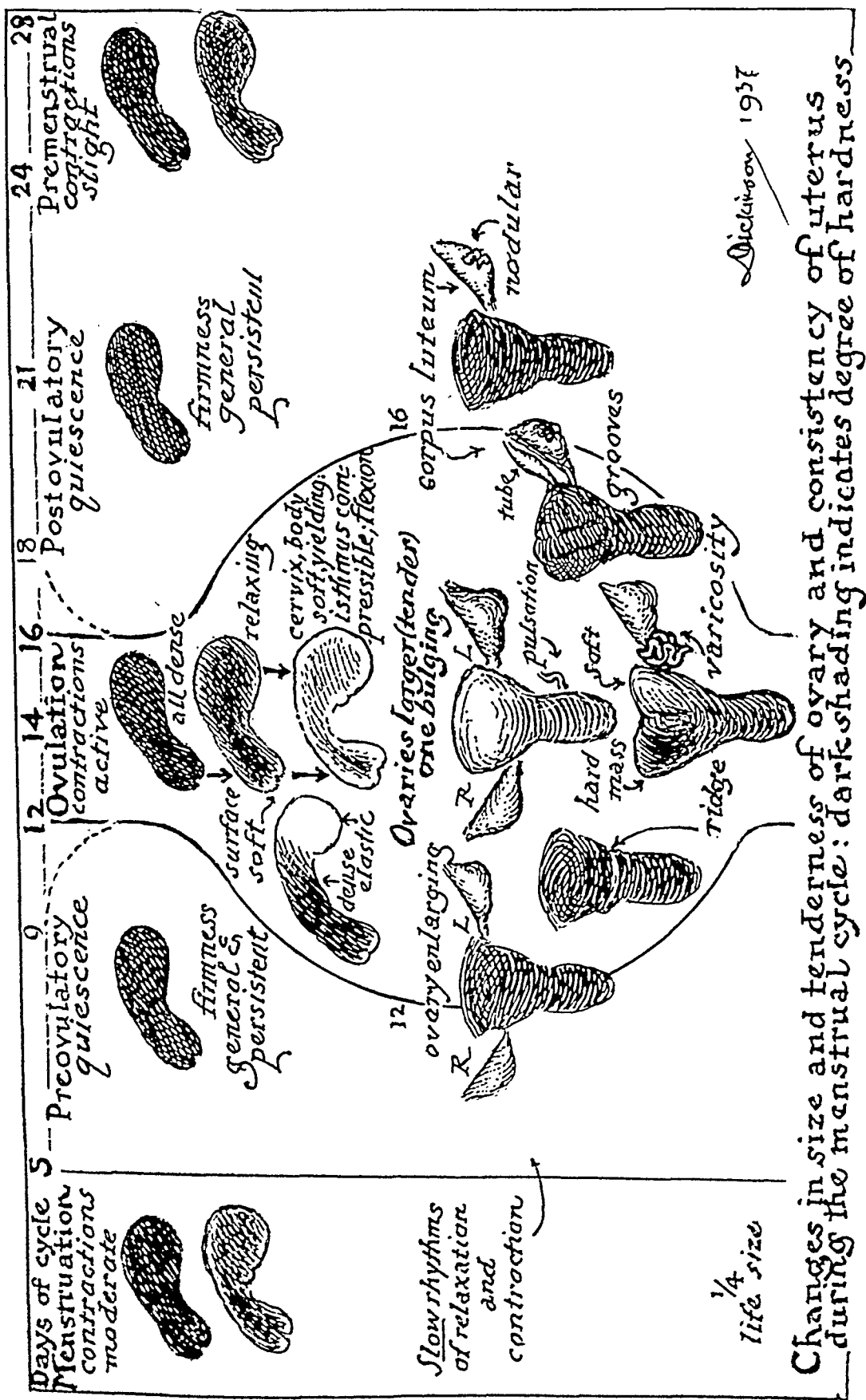
Posture is important. The tilting table that tips the trunk into a steep Trendelenburg may give what a level posture will not.³ Full support of abducted knees relaxes circumpelvic tensions. The lower leg lifted level on Goepel troughs under calf and knee works better than the feet at the table level, provided the apparatus is comfortable. In some women with a cushion under the buttocks, full flexion of thigh on trunk gives high reach because of relaxed belly walls, while in some women the thighs press on the abdomen and increase tension. In other words, intelligent choice and individual adaptation may make the difference between an ovary completely defined and one quite elusive.

The substance of the previous study was as follows: It covered 89 observations on 5 patients chiefly during the interval. Both ovaries were found to show swelling and tenderness, but one much more than the other, even enlarging to twice the size. A *protruding rotundity* could be outlined in about half the instances, and a few days later, a nodular smaller lump, like one side of a blackberry. At the latter stage the tube on the corresponding side might be thickened.

At the time of unilateral ovarian enlargement the uterus in clear-cut examples showed a marked alteration in consistency, not unlike that in early pregnancy. Softening of the isthmus, the old Hegar sign, or my signs, the nodular feel of one upper angle, or any one of a variety of ridges or grooves might be present.

These grooves, lengthwise and transverse, on corpus, isthmus or fundus, and the nodular or cornual asymmetries⁴ are confirmed by the x-ray shadows that depict clearly the striking alteration of the form of cavity of corpus and cervix during the waves of relaxation and contraction, general and local. These forms of cavity are carefully summarized in diagrams in Figs. 30 to 33 in *Human Sex Anatomy*. The chief change was *contraction and relaxation in a rhythm* running from 2 to 10 or even twenty minutes. During contraction any flexion, normal or marked, wholly or partly straightened out. A wave of contraction can start at the soft cervix and pass to isthmus and corpus. There can be complete softening of the whole organ except a core of cervix.

Before and after this rhythmic behavior in the midinterval, there are usually zones of complete quiescence which are almost diagnostic. During menstruation and preceding it, a minor capacity for these changes in consistence exists. In well-marked examples the difference in anteroposterior corpus diameter at the midinterval may be as much as one-third. Palpation of the uterus under favorable conditions



is easier than palpation of the ovaries, but it involves patience in all slow-acting musculatures. Erotic arousing does not seem to affect the phenomena. The much exploited rhythms in orgasm fall in the class of erotic fiction until evidence by trained observers is submitted.

Frequently in my histories the pronounced swelling and acute tenderness is labeled *ovaritis*, recurring *ovaritis*, even alternating *ovaritis* or *salpingitis*.

A new point is the vacillation of *varicosity* of the broad ligament with a pronounced unilateral finding at midinterval, and a change from side to side in sequent months. My form of examining table that allows a wide range of tilt permits emptying and filling of the vessels and confirmation of the diagnosis.²

For observation of the midinterval, conditions are favorable with gynecologists who give to the pessary a fair trial in those mobile retroversions which produce symptoms, then watch the results. They are especially favorable when teaching intelligent patients to do most of their own watching of position and pessary and ovarian tenderness. By self-diagnosis of relapse, by self-reposition and self-placement, the patient in many cases is enabled to leave the pessary out except when discomfort gives her notice, or the special relaxations and congestions of the period and of the midinterval are on, or when a long motor trip or a horseback ride calls for support, the pessary being used as needed, until pregnancies are behind her and the question of suspension calls for decision. In all these cases the ovulation period can be the time of election for special observation of the dependability of a "rhythm" and "safe period" for the particular individual.

The ovaries have been supposed to alternate in functioning, and this may be true, as Morse shows in rhesus monkeys.^{4a} The higher position of the left ovary may account for the fact that in Case 1, tenderness at ten to twenty-three days was found on the left side nine times, on the right twice, in the center twice.

I was fortunate in being able to find, in a university neighborhood close to my residence, five intelligent women volunteers meeting the above specifications who, on the way to market after breakfast, stopped in about every second day, especially at the midinterval, for three periods. Gratitude and scientific interest on the part of wife and husband, together with the desire to estimate the safe period, brought this to pass. In research done in a clinic one would pay patients at the end of each ten or fourteen days, as our Committee did with the daily vaginal smears done at the Woman's Hospital by a technician under Dr. Papanicolaou.

As the pelvic findings of two of the cases have been pictured rather fully in my book entitled *Human Sex Anatomy* and as one of these cases

Thus putting together fifty months of record and 33 observations involving (a) bimanual examination of ovaries; (b) interval tenderness, self-observed; and (c) spotting, the *scattering is wide, involving every day of the cycle from the tenth to the twenty-third*. There is a grouping of enlarged ovary and tenderness in the expected space between the eleventh and the fourteenth days, 11 items; and a second minor grouping on the twenty-first day, 3 items; and with 4 spottings grouped hereabouts also. Among the 11 notes on tenderness, the averages run fourteen days after beginning of period, fifteen days before the start. Erotic rousing (without male), well marked or with self-relief, has 26 notes, scattered, with 10 after the period, and 7 near the twenty-first day.

There are all degrees of rhythmic contraction at ovulation time, apparently. The most complete example found in my short series was deliberately selected and used in both my previous publications in order to exhibit all the points. Here is an example on the opposite end of the scale, including a picturesque occurrence seen only once.

CASE 2.—At the twelfth day one ovary was found to be nearly double the size of its fellow. At the fourteenth day, with the two fingertips of the right hand easily holding the right ovary against the firm right pelvic wall, a small grape collapsed, and this ovary became about the size of its fellow. Two days later the area seemed nodular, but by no means as clearly so as in patients examined later in the cycle. The uterine contractions were very slow and not easy to elicit on these first two examinations, with twelve minutes to soften the isthmus and thicken the corpus, and 2 to 4 to harden and shrink. It is my guess that this condition was part of a generally defective tone of muscle and vessel. Though showing high fertility, fair menstrual regularity and strong sex desire, this lady presents general muscular flabbiness, while her uninjured pelvic floor all but sags. It was noted in removing a dermoid before her pregnancies that the pelvic tissues everywhere showed markedly relaxed vessels. Thus sluggish uterine musculature and venous stagnation might be called upon to explain torpor in rhythms, particularly lack of that striking alteration in thickness supposed to be largely due to filling and emptying of the layer of meshed vessels beneath the outer muscular layer which is clearly depicted by Bayer.⁵

Rouget,⁶ in 1858, found the uterus thicker anteroposteriorly at menstruation and ovulation, but did not note the vacillations; he demonstrated that, postmortem, by complete filling of the vessels, one could double the size of the organ.

CASE 3.—This patient gave opportunity, in early pregnancies and while watching the pessary between pregnancies, to compare four findings of consistency of the uterus at the sixth week of gestation with the findings at seven midintervals. As the follicle grows very large in this patient, with the ovary sometimes as big as the fundus, it is favorable for comparison, twice as discovered on the left and three times on the right, with one temporary tubal thickening accompanying the ovarian enlargement of the same side.

Only once have I been able to hold a naked uterus in my hand (at laparotomy for suspension) and detect active contraction. It is presumably the anesthesia that arrests this activity, while the speed of our operative process defeats a watchful wait of ten minutes for observation. Monkey laparotomy might demonstrate the point.

Among my old histories I find 287, the first in 1886, in which the diagram and the accompanying notes show the uterus varying markedly from the usual consistency, ranging from that of the raw potato to or

in twenty days the patient received 8 injections of dimenformon, each containing 50,000 M. U., a total of 400,000 M. U. After this treatment, she was injected with 5 Rab. U. of progesteron daily from the twenty-first to the twenty-sixth day.

Analysis of the morning urine on the twenty-seventh day was positive. Thus this treatment did not decrease the elimination of prolan A.

Two days after the treatment a real menstrual bleeding began, lasting five days.

Result.—Combined treatment with follicular hormone and corpus luteum hormone induced menstrual bleeding. But it is not possible to influence increased elimination of prolan A.

CASE 4.—R. B., twenty-six years old, married five years. The patient never menstruated.

On April 1, 1935, before beginning the treatment, urinalysis was positive. There were at least 111 M. U. of prolan A demonstrable per liter of morning urine.

First treatment: From April 3 to April 22 the patient received 9 injections of dimenformon, a total of 450,000 M. U.

On April 23 urinalysis was positive; there were at least 111 M. U. of prolan A per liter of morning urine.

After this treatment, the patient received 5 Rab. U. of progesteron daily from April 23 until 26, a total of 20 Rab. U.

On April 26 the patient menstruated for the first time, the flow lasting four days. On the first day of the bleeding, one strip of mucous membrane was taken from the uterus with a special curette. Examination revealed a real premenstrual mucous membrane. The glands were rich in glycogen.

On April 29, the third day of menstruation, urinalysis for prolan A was again positive.

Second treatment: From May 2 to May 21 the patient received 9 injections of dimenformon, a total of 450,000 M. U. In addition she received 5 Rab. U. of progesteron from May 22 to May 26, a total of 25 Rab. U. On May 26 there was a menstrual bleeding again. On June 27, the second day of menstruation, urinalysis was negative, which means that 111 M. U. of prolan A were no longer demonstrable.

Result.—Though menstruation could be induced, it was not possible to decrease excretion of prolan A by administering dimenformon and a following treatment with progesteron, respectively. After the second treatment, i.e., during the second menstruation only, was elimination of prolan A decreased.

CASTRATA

CASE 5.—G., twenty-eight years old. She had been castrated because of bilateral tumors five years earlier. The patient suffered very much physically and psychically from the deficiency symptoms. The vagina was narrowed and pale; the uterus was hypoplastic, 4 cm. long. I observed the patient for a year. By hormonal treatment I succeeded in inducing bleedings at regular intervals. Her complaints stopped completely. During the first months (December, 1934 to March, 1935), bleeding was induced by a combined treatment with dimenformon and progesteron. Within twenty days the patient received 7 injections of dimenformon, a total of 350,000 M. U. During the next four days she received 5 Rab. U. of progesteron daily; two to three days later there was a regular menstrual bleeding which lasted three to six days.

In April and May, 1935, I was contented with inducing pseudomenstruation. Within twenty days the patient received 350,000 M. U. of dimenformon, and after seven days flow began. It is interesting to note that there was always a week's interval after the administration of follicular hormone and the beginning of the flow.

RESECTION OF THE PRESACRAL NERVE IN THE TREATMENT OF OBSTINATE DYSMENORRHEA

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RESECTION of the presacral nerve, which I performed for the first time in December, 1924, is now regarded favorably by many surgeons. Judging from the literature on the subject, it may be said that it is now adopted in almost every country in the world. It seems, however, that while the operation is winning converts each year in France, in foreign countries its use is still confined to a small minority. The number of women, therefore, who are able to benefit from this procedure, remains still limited. After an experience of twelve years with the operation, I may say that I am more and more convinced of the value of resection of the presacral nerve in every syndrome associated with an anatomic or functional disturbance of the hypogastric plexus, and that I know of no other therapeutic method that may be substituted for it. Adson, one of the last converts to presacral sympathectomy, declares too, in a recent article, that, after having observed the results obtained, the operation seems to him much more valuable than it did at first. Indeed, of all the surgeons who have performed presacral resection correctly in cases in which the operation was indicated, I do not know one who abandoned it later. In general, it may be said that, whenever the indications were properly observed and the operation correctly performed, the results conformed to those I described in my first communications.

I shall not, at this time, discuss either the technic or the indications for the operation, but refer those interested to the various reports I presented on this subject, in particular to the general study made in my book *Chirurgie du Sympathique pelvien en Gynecologie*¹ or in the *Journal International de Chirurgie*.² I intend to confine myself here to a discussion of some ideas on the treatment of severe functional dysmenorrhea, which is one of the most common indications for resection of the presacral nerve.

Normally, in most women, menstruation is unaccompanied by painful sensations. The evolution and maturation of the graafian follicle and its rupture which, in the majority of cases, precedes the thickening of the uterine mucosa in preparation for the embedding of the ovum, as well as its destruction, in the absence of fertilization, cause neither serious discomfort nor pain. The autonomic nervous system seems to remain indifferent to the biologic phenomena, marking the different stages of the menstrual cycle. Why then, are all these physiologic

toward that of the ripe tomato, in whole or in part, in the same person. The most frequent finding is the compressible isthmus, the next the thickened, rather soft or very elastic corpus, with the supravaginal cervix generally maintaining its rigid incompressibility. The grooves and the hard lump in a half-corpus are sometimes present. Unhappily, the exact day of the cycle is infrequently stated.

SUMMARY

Under specified favorable circumstances bimanual palpation in women can detect changes in the ovary and uterine contraction which point to the time of ovulation or omission of ovulation. The tenderness is often such as to suggest ovaritis or salpingitis. Varicosity of a broad ligament may be present only, or accented only, at the mid-interval. In one patient with a five-year report, symptoms, Mittelschmerz, spotting and self-detected tenderness, were scattered from day ten to day twenty-three. In another the nonpregnant uterus of the midinterval copied her six weeks' pregnancy findings.

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numerous sympathetic fibers in the cervix and the uterosacral ligaments. Last, I may add that the concept of stenosis could not explain "painful amenorrhea" to which Dalehe has drawn our attention, and which is characterized by painful periodic attacks at the date when menstruation should take place, even when there is no serous or bloody discharge from the uterus. I have, on several occasions, operated upon such patients in whom dysmenorrhea alternated with painful amenorrhea. I found no lesions of the genital tract that could explain the phenomenon.

In view of these facts, and the frequent failures following dilatation and curettage, I was led to seek another form of therapy. Having had the opportunity of observing a certain number of patients in whom the dysmenorrhea was associated with other complaints indicating a dysfunction of the sympathetic nervous system, e.g., dyspareunia, vaginismus, cystalgia, sensation of burning on urination, tenesmus ani, vaginal pain, pruritus vulvae, sexual hyperexcitability, I was led to do, at first, periarterial sympathectomies of the hypogastric arteries, and later, resection of the presacral nerve.

Former authors would explain all these phenomena collectively or separately, on the basis of a neurosis, anxiety-neurosis, neurarthrit, spasmophilia or hysteria. Today, they are generally attributed to a dysfunction of the autonomic nervous system, the abnormal hyperexcitation or hyperexcitability of which is responsible for the symptoms enumerated above. According to this concept very slight injuries of the genital organs and even remote pelvic lesions may sometimes provoke, either by direct irritation or by reflex action, sensory-motor or vasomotor disturbances in the pelvis, and cause pelvic neuralgia, dysmenorrhea or cystalgia, etc. Furthermore a very slight anatomic injury of an ovary, or of the endocrine glands connected with it, and even a simple disturbance in the evolution of the graafian follicle (the hormones of which exert an influence not only on the uterine mucosa and uterine contractions but also on the vagosympathetic nervous system itself) initiate, by reflex and endocrine stimuli, vicious circles which continue to persist until they can be interrupted. Last, it enables us to understand how a primary disturbance of the pelvic sympathetic system (hypogastric plexialgia or plexitis) or of the nervous centers connected with it, can lead to the same results.

Doubtless, this theory of the pathogenesis of dysmenorrhea is not immune from criticism, but it is justified by the fact that, while dysmenorrhea and pelvic neuralgia do not respond to the most varied operations on the ovary or the uterus, these conditions are generally completely cured by properly performed presacral sympathectomy.

As regards so-called essential dysmenorrhea, of nearly 300 patients upon whom I operated in the course of twelve years, I know of only two that were not relieved.

phenomena characterized in certain women by pains that necessitate rest in bed, cessation of work, and the use of narcotics? Under what influence does the autonomic nervous system, which remains in some way impassive in the course of repeated cycles, acquire such a hyper-irritability as to cause severe pain associated with the preparation and shedding of the endometrium?

Former gynecologists attempted to explain this fact by the existence of a cervical stenosis or of an endometritis which they treated by dilatation and curettage. Simple explanations appeal to us most, which may account for the favor accorded this theory until recently.

However, one has but to examine the facts more closely to realize that usually at the onset of functional dysmenorrhea, there is neither endometritis nor a stenosis of the cervix or of the isthmus. Doubtless, before we were acquainted with the evolution of the uterine mucosa, the premenstrual hyperplasia observed in cases in which a curettage had been performed, might have been taken for an inflammatory lesion of the endometrium, but we know today that the latter is in reality dependent on the ovarian hormones. And the best proof that inflammation does not seem to play a great rôle in the occurrence of dysmenorrhea, is that most cases of adnexitis develop without ever causing severe or stubborn dysmenorrhea.

The arguments that can be advanced against a mechanical cause of menstrual pains are still more numerous. Without discussing here the observations of some gynecologists who have sought in vain for a stenosis or a spasm of the uterine isthmus, it is an irrefutable fact that severe, stubborn dysmenorrhea which requires surgical intervention is almost always secondary in origin.

Actually, in most cases, we deal with girls who menstruated normally for one, two, three, or four years and sometimes longer and then began to experience such menstrual pain that they were forced to take to bed. Sometimes this occurs after acute serofibrinous pleurisy that developed without complications, or after erythema nodosum, or any other attenuated tuberculous manifestations without there having been any localization of tuberculous lesions in the ovary or the uterus. But generally, the most careful inquiry into the history reveals no cause for the occurrence of the dysmenorrhea. If we add to this the fact that the most thorough dilatation, and even parturition, is not always sufficient to cure menstrual pains, then one is forced to give up the idea of stenosis as a causative factor. I am well aware of the fact that menstrual pains often assume the character of true uterine colics and that in about half the cases dilatation of the cervix causes them to disappear. One, however, is not justified in assuming a relationship between the stenosis and the dysmenorrhea, for one may obtain with dilatation of the anus as good or better results. It is highly probable that the method works by stretching of the very

ago relieved all her symptoms. The patient gained nine pounds in three months after the operation and seventeen pounds during the ensuing year. After having remained six years away from home, she was easily acclimated to her birthplace which she has never left since. Quite recently she wrote me, "It is to your operation, dear Doctor, that I owe my return to my family and my active life, there. I shall always be very grateful to you." Since at the time of the operation I could discover no pelvic lesion, it was obviously a case of functional dysmenorrhea.

Another case, a girl aged twenty-eight years, was under treatment in the mountains, for very serious pulmonary lesions and a cavity of the right lung. After fifteen or eighteen months, as the pulmonary condition began to improve, the patient, whose menstrual periods had never been painful, began to suffer from dysmenorrhea so severe that during the week of her flow she rapidly lost the two or three pounds which she had gained in the preceding three weeks. When I saw her for the first time, she was not yet in good enough general condition to allow me to operate. I stated, however, that the occurrence of dysmenorrhea should be considered as a favorable prognostic sign. I have never seen dysmenorrhea appear this late in the course of tuberculous disease which went on to a fatal outcome. Some months afterward, the pulmonary lesions being no longer active, I resected the presacral nerve. From that time the cure proceeded rapidly. The patient, who weighed only 80 pounds, now weighs 130 pounds, and she no longer suffers during her periods.

In passing, I may mention that there were a number of cases of young girls who had had an appendectomy to relieve the dysmenorrhea. These, in the face of the steadily increasing pain, consented to a second intervention, though not without reluctance, because of the disappointing results of the appendectomy which they felt, moreover, had aggravated the dysmenorrhea. This second operation brought a complete and definite cure to the dysmenorrhea. Many of them married and are now very happy mothers.

It is not only from a pathologic point of view that resection of the presacral nerve has a good effect in relieving dysmenorrhea. In another article, I described the case of a girl, the sister of a surgeon, who was obliged every month to remain in bed at the time of her periods. Two years after the operation (which her brother had long hesitated to advise, always hoping the condition would finally subside) she wrote to thank me. Had she not been operated upon, she would not have passed her examinations as a nurse, for on the examination day she would have had to remain in bed. She was operated upon four years ago and was completely relieved of her pains. She now leads an active life as a district nurse without ever being incapacitated.

I also quoted the case of a girl, aged nineteen years, the daughter of a well-known physician. Her dysmenorrhea began after acute serofibrinous pleurisy that developed without complications, and she had such painful paroxysms that for forty-eight hours she was obliged to stay in bed and was not relieved by any drug including belladonna, papaverine, and all the opiates used in such cases. She would vomit a great deal; the temperature during the forty-eight hours would remain at 40° C. and would return to normal at the end of the painful period. Several times, this girl, who was very athletic, had stopped during the winter in the mountains and while there she had suffered from attacks of painful amenorrhea. Professor Maranon, when consulted, had attributed her symptoms to a dysfunction of the

In the first case the patient was sympathectomized elsewhere by an excellent surgeon, but no doubt the resection had not been complete, and he had resected only the left part of the nerve, for I found on this side a cicatricial neuroma, the histologic picture of which I presented in my book. After the operation, the patient, who had been suffering continually from the neuroma, was at once relieved. Some months afterward, however, the periods again became painful. This led the first surgeon to castrate the patient.

The second case is more interesting. It was a girl, aged twenty-four years, who for five years had suffered from dysmenorrhea, refractory to all medical measures. In addition, for three years, the patient experienced intense sexual hyperexcitation, nymphomania and pruritus vulvae not explained by any local or constitutional cause. She was operated upon in 1934 and pruritus vulvae and sexual hyperexcitation disappeared completely. Unfortunately, the dysmenorrhea was not influenced. The patient continued to suffer at the time of her periods and I had to do a temporary x-ray castration.

During the laparotomy in this case, I had found signs of peritonitis in the culdesac with adhesions between the rectum and the posterior wall of the vagina, and some free peritoneal fluid. Can one ascribe the persistence of the painful periods to these findings? I do not think so, since if the local inflammatory process had been the causative factor, it seems probable that the pruritus vulvae and sexual hyperexcitation would not have disappeared. It is possible that the inflammatory reaction was due to an endometriosis that escaped me. In any case one cannot claim that the presacral nerve had not been removed or only incompletely, for resection had been particularly easy in that case.

Besides these unsuccessful results, three or four other patients still suffer during their periods, but only during one or two hours, instead of twenty-four or forty-eight hours, and in no case are they forced to stay in bed or stop work. While these were not completely successful, the results, however, were highly satisfactory to the patients.

In contrast to the few cases which were not as fully relieved as I had expected, resection of the presacral nerve led to a complete cure in all the other cases. It is impossible to present here, even in abstract form, all the facts relevant to these cases. I will confine my remarks to some of them that were particularly striking.

The following case affords an example: A girl, aged twenty-two years, menstruated from the age of fourteen. Her periods were at first normal, later on they were accompanied by more and more severe pains, which finally impaired her health. As a child, the patient had had a bronchitis which resulted in pulmonary sclerosis. For this reason, during six years, since she could not bear the climate of her birthplace by the side of the Loire, she led a rather unhappy life in various preventoria. One day the Director of the sanatorium where she was being treated, seeing how severely she suffered during her menstrual periods, sent her to me. As the pulmonary lesions were not active, I proposed operation. Her father was very unwilling to agree to this since two years before she had had an appendectomy for the dysmenorrhea without any relief. But the operation seemed to me all the more necessary since for some months the patient had also developed pain in the vagina and nymphomania. Resection of the presacral nerve performed five years

ovarian nerves. This is so striking that we sometimes see patients with both menstrual and intermenstrual pains, in whom following resection of the presacral nerve, ovulation alone remained painful, the menstrual periods causing no discomfort. In these cases, complementary resection of the ovarian nerves is sometimes necessary. Resection of the lumbo-ovarian nerves, or the "isophenolization" of the uteroovarian plexus has not always, in my experience, given satisfactory results.

I wish to point out that in a number of the cases reported in the literature as unsuccessful, failure has been due either to incomplete resection of the nerve or to the fact that the operation was not indicated in the cases chosen.

The mortality rate is that of all simple aseptic abdominal operations, about 1 per 100. In more than 300 operations I lost only two patients who died from acute pulmonary complications. I never noted any abdominal complication immediately or subsequently, and I never observed trouble with the sphincters or with the genital organs. More than 50 patients have had consecutive pregnancies and no accident was ever noted during parturition.

In the absence of precise and certain physiologic data concerning the nature and origin of the constituents of the presacral nerve (superior hypogastric plexus of Hovelacque), it is difficult to explain the successful results of presacral sympathectomy. Is it due to the suppression and interruption of abnormal sensory-motor reflexes or modification of the pelvic circulatory system? Both theories can be postulated. Adson states that dysmenorrhea as well as the other genital disturbances for which operation is required, are produced by abnormal stimuli from superior autonomic nervous centers of the midbrain which are connected with the pituitary gland. Resection of the presacral nerve is effective because it suppresses the connections of the genital organs with the nervous centers. However hypothetical those theories may be, it is quite certain that in the syndromes of hypogastric plexalgia, and particularly in dysmenorrhea, which is the most frequent manifestation of its dysfunction, well-performed pelvic sympathectomy yields uniformly good results. Accordingly, when all of the known therapeutic measures have been ineffective, it seems wisest to advise early operation. Furthermore, there is the possibility that a slight anatomic lesion (ovarian endometriosis, adenomyosis of the cornua for instance) which had not been discovered by clinical examination may be found, treatment of which will be sufficient to relieve the dysmenorrhea. But in the other cases, resection of the presacral nerve will effect a cure in patients who have been refractory to all other forms of therapy.

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anterior lobe of the pituitary gland and prescribed treatment with prolan. This form of therapy was ineffectual. I was then called in consultation and resected her presacral nerve without any additional surgical procedures. Following this her symptoms disappeared. She was operated upon two and one-half years ago and she has not suffered during her menstrual periods since then. She was married last year and has now been pregnant for four months.

These few instances, recalled from about 300, are typical. One can best judge the value of the operation by the results obtained in cases of membranous dysmenorrhea. The refractory character of this type of dysmenorrhea is well known. The pain experienced, together with the expulsion of fragments of a thickened mucosa (menstrual decidua), occasionally simulates a miscarriage. I operated upon a patient who in spite of two previous deliveries still suffered during her menstrual periods. She was operated upon five years ago. Since then she has had no complaints, although she still expels large pieces of mucosa during her periods. She had another normal pregnancy and an interstitial pregnancy for which Convert, of Bourg, performed a conservative operation.

In another case (my youngest patient) a girl, aged fourteen years, menstruated from the age of ten. Her dysmenorrhea (membranous) was so painful that at thirteen she was obliged to leave school. Here again, resection of the presacral nerve, by curing the dysmenorrhea, enabled her to continue her studies, to pass her examinations, and become a chemist.

I could cite many other interesting cases. It is sufficient to say that in the treatment of severe dysmenorrhea, no other method has ever given such consistently good results.

It is a popular belief that marriage will frequently relieve dysmenorrhea, which is indeed true in many cases in which the menstrual pains are easily controlled with the usual sedatives and which are not severe enough to incapacitate the individual. However, in severe dysmenorrhea not relieved by opium, belladonna and such opiates, which necessitates rest in bed and is accompanied by sympathetic disturbances, conjugal intercourse does not relieve the condition and the coital act is frequently difficult and painful and only adds one more tribulation to the life of these patients. I believe, therefore, that it is preferable to operate upon them without exposing them to this distressing trial.

I wish to emphasize that resection of the pelvic sympathetic nerve is suitable only in cases in which menstrual pains are not caused either by malformations or adenomyomas of the cornua or endometriosis of the ovaries, of the tubes, or of the rectovaginal septum, or any other still more evident lesion of the genital organs. It is valueless for pain of ovarian origin or intermenstrual pain which is associated with ovulation. This type of pain is generally not influenced by resection of the hypogastric plexus. This is to be expected since the ovaries receive their nerve supply from another pathway through the utero-

Prior to the introduction of excretory urography in 1929, it was impossible to follow these cases postoperatively intelligently and determine how well the reimplanted kidney functioned. Naturally, it was impossible to control the output in the upper urinary tract after ureterosigmoid anastomosis. Occasionally with the ureterovesical anastomoses, one should catheterize the reimplanted ureter and de-



Fig. 1, A.

Fig. 1.—Case 1, P. L., aged fifty years. A, Retrograde pyeloureterogram before operation, showing dilated pelvis and obstructed lower ureter, ending in bulb. Picture taken seven hours after injection of iodide solution. B, Excretory urogram before operation, showing practically same condition with bulbous lower end of right ureter. C, Excretory urogram four-plus weeks after ureter neostomy, showing right kidney pelvis much smaller and ureter filling all the way down to bladder, only moderately enlarged. D, Excretory urogram almost five years after right ureter neostomy, showing marked reduction of the hydronephrosis, practically normal ureter throughout.

THE VALUE OF URETERAL IMPLANTATION INTO THE BLADDER AND INTO THE SIGMOID IN GYNECOLOGIC INJURIES AND DISEASES

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FORTY-THREE years ago, Florian Krug of New York stated that "accidental injury to the ureters is one of the most unfortunate occurrences of abdominal surgery . . . the almost universal adoption of the Trendelenburg posture has greatly reduced the liability to this accident, as it enables us to operate under the guidance of the eye as well as of the touch. Still, there are cases, and always will be cases, where, owing to the nature of the disease, or some anomaly of the relative position of the ureter, injury to this organ is unavoidable."

In case of such injury, if detected during the operation, naturally an immediate reimplantation of the ureter into the bladder should be done, if possible. These cases present a group with which the gynecologist has to deal immediately, and are rarely seen by the urologic surgeon. The names of Krug, Baldy, Stoeckel, Franz, Kroenig, and Sampson are intimately connected with the development of this branch of surgery. Not only did they have the opportunity to perform an immediate repair to the damaged condition, but often, after recuperation from the first abdominal procedure, they had the opportunity to correct the fistulous leak resulting from damage to one or both ureters.

In the following brief paper, I shall refer to the three types of gynecologic patients, who from time to time seek urologic surgery for the relief of disturbances in the ureter, caused by operative interference in the pelvis by the gynecologist, by disease in the pelvis (parametritis), as well as those cases of incurable vesicovaginal fistula, which are, despite numerous attempts at closure, passing all their urine through the fistulous opening.

Through close association with the gynecologists, one is able, perhaps, to see more of these cases than is the lot of most urologic surgeons. The cases about to be reported are grouped as follows:

Group I.—Cases of compression stricture of the ureter due to parametritis and periureteritis, in which neostomy is necessary to relieve the painful condition in the kidney and get adequate drainage of the obstructed hydroureteronephrosis.

Group II.—Cases of ureterovaginal fistula, caused by damage to the ureter in either pelvic or abdominal procedures.

Group III.—Cases of large, incurable, vesicovaginal fistula, in which the ureters have to be implanted into the sigmoid, to deflect the stream of urine.

On June 9, 12, 16, 19, 23, 26, 29, 1935, respectively, the patient received one ampulla of dimenformon containing 50,000 M. U. Analysis of the morning urine of June 14, after administration of 100,000 M. U., was positive. That means, that there were at least 111 M. U. of prolan A per liter of urine demonstrable. A second analysis was made on July 3, three days after stopping treatment. This analysis, too, was positive. Besides prolan A, prolan B was also demonstrable. (111 M. U. per liter of urine.)

On July 6 occurred another bleeding. From July until December, 1935, there used to be bleeding, starting regularly seven days after closure of the treatment with dimenformon.

Result.—In a young castrated woman increased elimination of prolan A could not be impaired, though she was treated with hormones for seven months. Menstruation or pseudomenstruation, respectively, had been induced on seven occasions. In spite of the intensive treatment, no influence on elimination of prolan could be obtained.

DISCUSSION

Accompanying the loss of the ovarian function (primary and secondary amenorrhea, third stage of climax, castration) there is an increased elimination of prolan A in the urine. How can this be explained? When, during the climax, the ovarian tissues cease to function, prolan A loses its effect on the ovary and is unable to produce folliculin. This phenomenon might be explained by the fact that prolan A, having thus become useless, is now being excreted with the urine.

The following explanation seems to me much more essential. The gonadotropic hormones are superordinate sexual hormones. The ovary regulates the function of the anterior lobe of the pituitary by stimulation or by retardation. As I reported a short while ago elsewhere,⁵ follicular hormone is able to inhibit important functions of the anterior lobe of the pituitary. It is easy to imagine that the anterior lobe, being deprived of its checking apparatus, would produce an excess of hormones which would be excreted with the urine. This opinion is supported by H. M. Evans⁶ who proves that the pituitaries of castrated animals have a higher content of gonadotropic hormones. Possibly both causes cooperate, i.e., the absent working point for the gonadotropic hormone following loss of the ovarian function and the active hyperfunction of the anterior lobe of the castrate. To me, hyperfunction seems to be the more important cause.

A few years ago (1931),⁷ I was experimenting to find whether this hyperfunction might be moderated. At that time we did not yet possess hormones in strong enough concentrations. I performed a homoplastic transplantation of ovarian tissue in a young castrated woman. The increased elimination of prolan remained uninfluenced by this operation. There was also no effect on the prolan excretion after subcutaneous or intravenous injections, respectively, totaling 15,000 M. U. of folliculin. It might be argued against these negative findings that neither ovarian transplantation nor folliculin administration (15,000 M. U.) was sufficient to exert a depressive effect on the

termine, more or less satisfactorily, the function of the reimplanted organ. In this field, however, excretory urography has proved of inestimable value, as it not only gives the picture of the anatomical

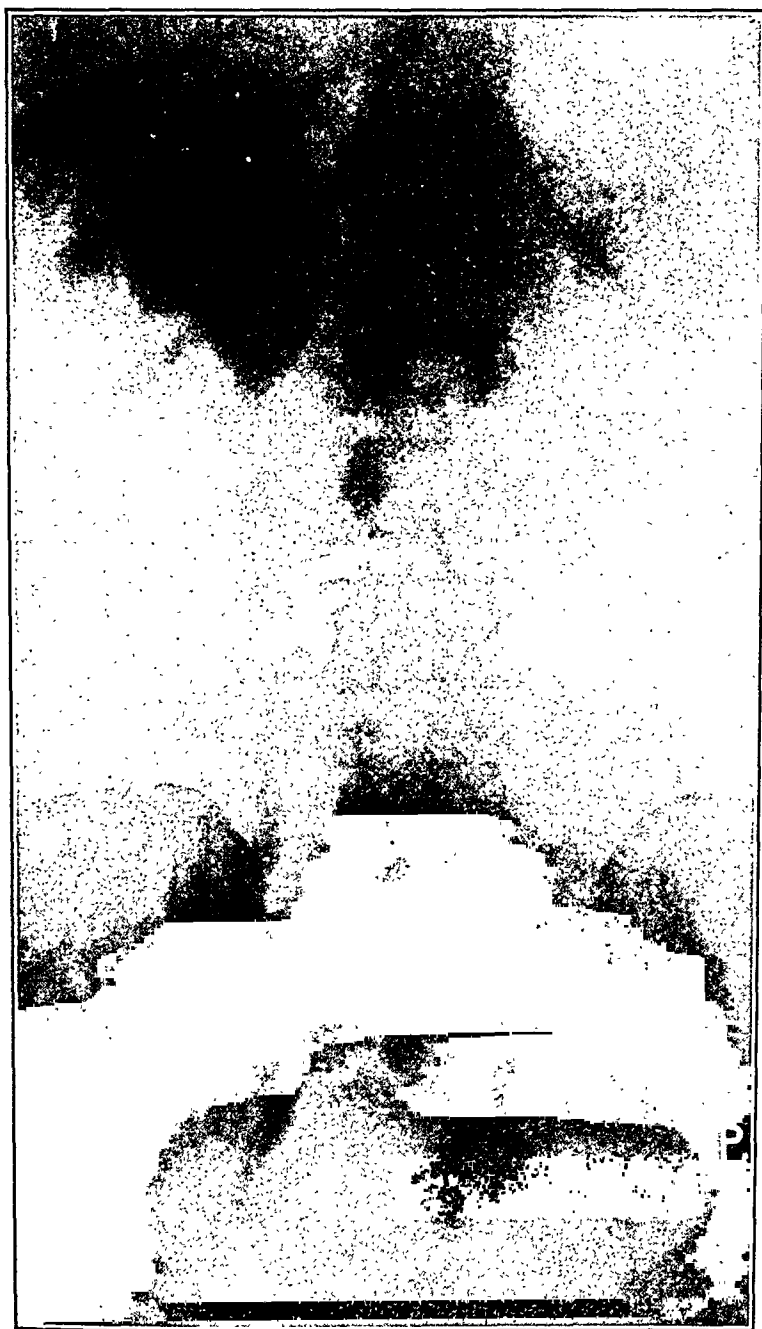


Fig. 1, B.

condition of the ureter and bladder, but at the same time gives a fair indication of the relative function of the reimplanted organ.

To illustrate these three types of cases, I have selected a series of three cases, that demonstrate rather conclusively the great value of conservative surgery under these conditions. The urograms are par-

ticularly instructive and, in some cases which have been followed for years after the ureteral transplantation, the roentgen studies are particularly illuminating.

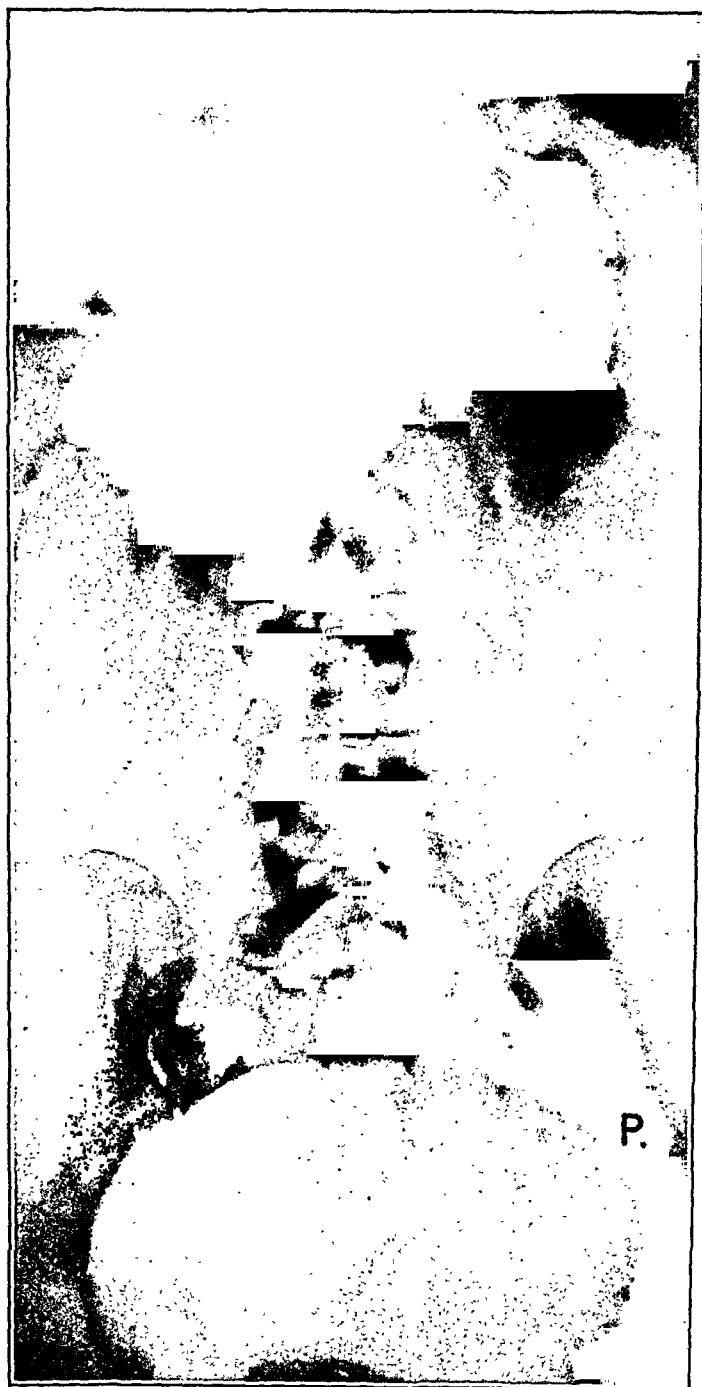


Fig. 1, C.

CASE 1.—Obstruction of the right ureter by periureteritis (parametritis), producing hydroureteronephrosis. P. L., aged fifty years. Retrograde urogram showed extensive dilatation of both ureters and kidney pelvis. Patient had recurrent obstructive symptoms on the right side, and the retrograde-filled right kidney did

not empty completely after seven hours. The lower end of the ureter was bulbous and dilated and remained so, despite stretchings continued over months. Excretory urogram showed the same ureterohydronephrosis with stricture in the right ureter close to the bladder. Jan. 5, 1932, right neostomy, extraperitoneal. Stricture found behind uterine vessels. Considerable periureteritis. Indwelling urethral catheter. Considerable urinary leakage from wound, as if ureter had pulled out. Tension



Fig. 1, D.

had been considerable at operation, the large thick ureter being freed retroperitoneally well into the lumbar gutter, and the bladder was mobilized as well. Jan. 25, 1932, cystoscopy, right ureter easily catheterized. Feb. 11, 1932, excretory urogram showed good function both sides. Feb. 27, 1932, chills, fever, frequency and right kidney pain and tenderness. Cystogram in Trendelenburg position showed no reflux. Symptoms subsided and on April 20, 1932, excretory urogram

showed right kidney emptied well and the ureterohydronephrosis was less marked Grade 1—plus. Sept. 10, 1932, cystoscopy, good indigo carmine at fifteen minutes from right kidney, No. 5 ureteral catheter passed to kidney pelvis and 15 c.c. clear urine aspirated. Dec. 4, 1936, excretory urogram showed practically normal ureter throughout, marked reduction of the hydronephrosis (Fig. 1, A-D).

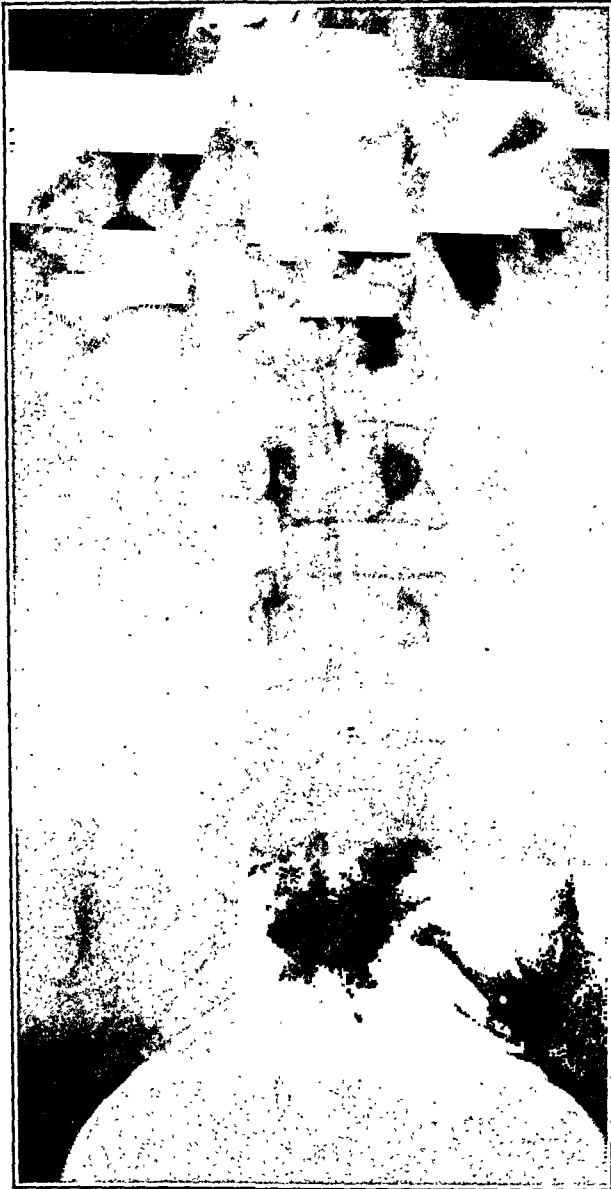


Fig. 2, A.

Fig. 2.—Case 2, H. M., aged twenty-three years. A, Excretory urogram ten months after left ureter neostomy, showing normal upper urinary tract. B, Excretory urogram two and three-fourths years after left ureter neostomy, showing ureters in pelvis absolutely normal in caliber, and on left side whole ureter is filled, as well as kidney, and calices showing normal contour. Impossible to distinguish between two sides as to which has been operated upon. C, Excretory urogram seven and three-fourths years after left ureter neostomy, showing good function both kidneys, ureter can be traced down to bladder, showing one dilated spindle over the sacroiliac joint, and another one just external to the bladder.

CASE 2.—*Ureterovaginal fistula following gynecologic operative injury.* H. C. M., aged twenty-three years. October, 1928, gynecologic transvaginal procedure, and ten days later vaginal urinary leakage. March 8, 1929, left ureter neostomy, extraperitoneal route. Bladder drained with a transurethral Pezzer catheter.

April 29, 1929, cystoscopy, left ureter catheterized, no indigo carmine at twenty-five minutes (intramuscular injection), specimen clear. Right kidney strong indigo carmine. Jan. 27, 1930, excretory urogram showed normal left ureter and kidney. Right pelvis slightly dilated. Dec. 8, 1931, excretory urogram showed absolutely normal pictures in both kidneys and ureters. Dec. 8, 1936, excretory



Fig. 2, B.

urogram showed normal left kidney, good function, and ureter can be traced down to the bladder, showing one dilated spindle over the sacroiliac joint and another one just external to the bladder (Fig. 2, A-C).

CASE 3.—*Vesicovaginal fistula, following cesarean operation.* G. S., aged thirty-six. In 1932, following forceps and cesarean operation, developed vaginal fistula, complicated by calculus in the bladder after the first attempt to close the fistula. The calculus formed about a foreign body. In all there were eight attempts at

repair, without success, so that in 1936 the patient was leaking vaginally and losing all her urine. Excretory urogram showed good function, normal anatomy in the upper urinary tract. Blood urea normal. After preoperative preparation with castor oil, colon irrigations, followed by constipating diet, on Feb. 4, 1936, a left ureterosigmoidostomy was carried out. By the ninth day following the implantation of the ureter, there was copious output of urine by rectum and before the

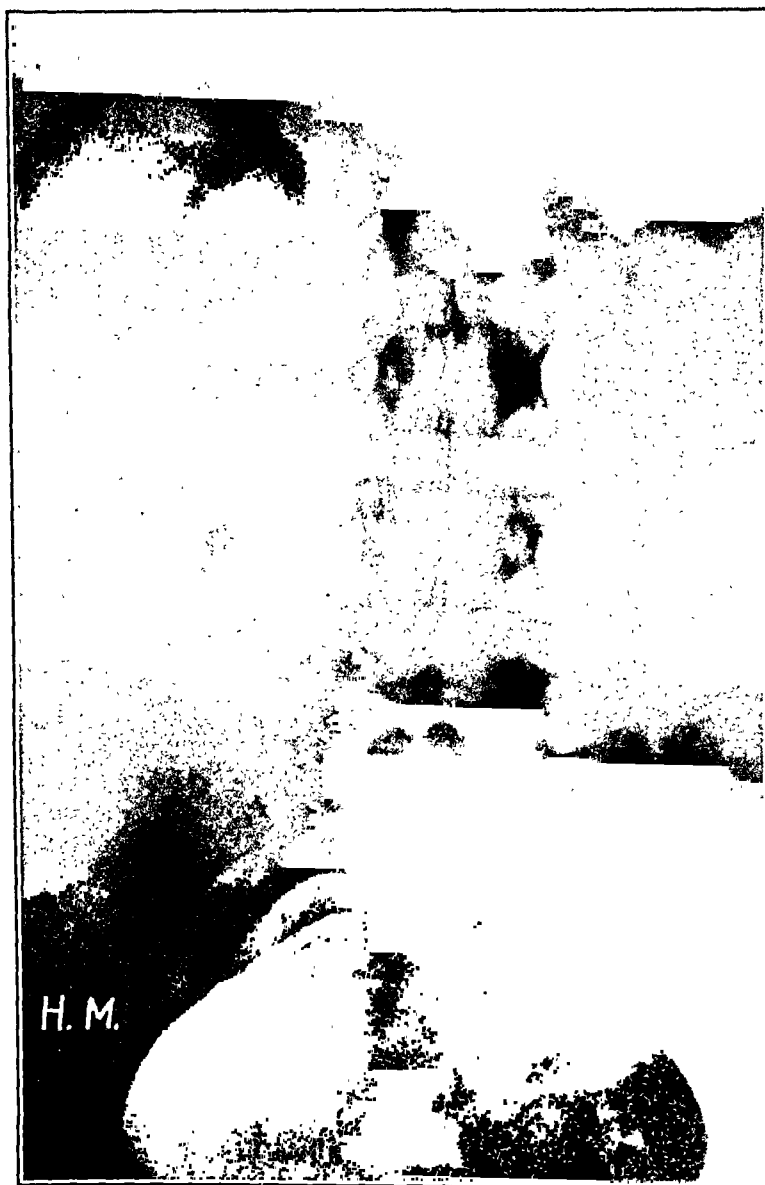


Fig. 2, C.

patient was discharged from the hospital, she was passing fluid movements, some of which were almost pure urine, four or five times a day with perfect control of her rectal reservoir. Excretory urogram was made on the twentieth day following the implantation of the left ureter, and showed a moderate left hydroureteronephrosis. On April 14, 1936, as the patient had no symptoms from the left ureter anastomosis, a similar anastomosis was made between the right ureter and sigmoid. Patient stood the operation very well, there was no serious reaction, and she made an uneventful recovery. At both of these operations, the split end of the ureter

was drawn with a mattress stitch of Pagenstecher into the lumen of the sigmoid, after incising the serosa and muscularis down to the submucosa and making a trough in the wall of the bowel by pushing these structures aside and burying the ureter with two layers of fine chromic gut, Lembert sutures. Pezzer catheter was left in the rectum. June 20, 1936, postoperative excretory urogram showed ex-

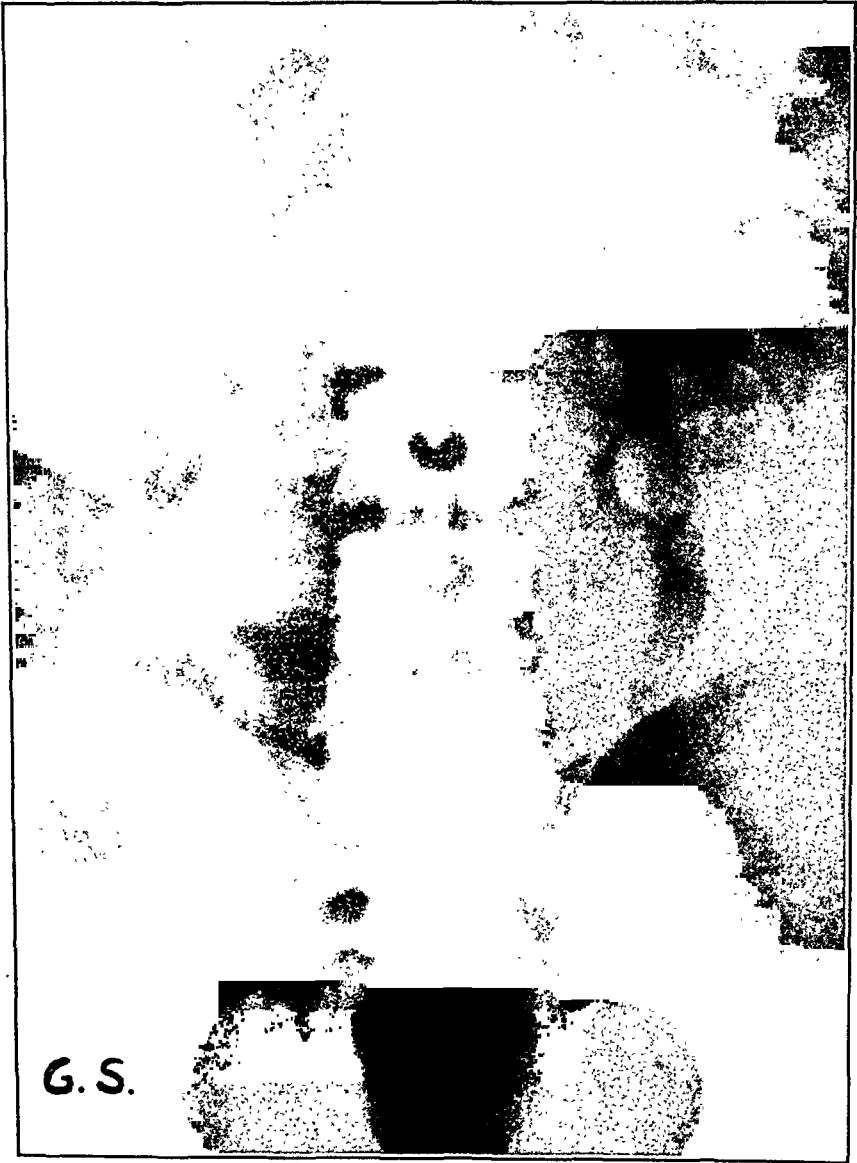


Fig. 3.—Case 3, G. S., aged thirty-six years. 4, Excretory urogram ten months following left uretersigmoidostomy, eight months following right uretersigmoidostomy, showing moderate hydroureteronephrosis.

cellent function of both kidneys. There was slight dilatation of the upper urinary tract, as one sees so regularly after anastomosis of ureter and sigmoid. This dilatation may gradually disappear and normal anatomy be reestablished. The patient has had no attacks of pyelitis, and rectal control is perfectly satisfactory. Excretory urogram on Dec. 12, 1936, showed moderate hydroureteronephrosis (Fig. 3).

THE PATHOLOGY AND TREATMENT OF INFLAMMATORY DISEASES OF THE CERVIX

“THE PELVIC TONSIL”

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THE cervix uteri is a halfway “stop” between two important highways. It is frequently the repository of the defects and weakness of both of these. It is influenced by the physiology and pathology of both of these avenues of approach. It is a barrier to infection, often suffering much in its defense of the sanctum uterinum. Unfortunately, it is situated in the very middle of the “silent area” of the pelvis—that territory bounded above by the peritoneum and below by the perineum, in which gross and grave pathology can, and does, exist without causing symptoms. This area, being part of the visceral field of the body, is almost devoid of tactile nerve endings (just as other intracorporeal viscera) and therefore pain—that announcer of physical ills—is quiescent in the pelvis, and disease may take hold and advance to incurable proportions before the victim is aware of its presence. The painlessness of cervical disease is proverbial. The delicate cervical columnar lining, set upon a functionally unchanging substratum of fibromuscular tissue, is in contrast to the ever changing uterine mucosa which sheds most of its sins of defect every month and renews its vitality with pregnancies. The cervical glands retain the surface scars of battle, the uterine mucosa casts them off—even the major scars of pregnancy. The cervical glands, racemose and deeply burrowing, become harbingers of infection by becoming retention cysts, and inflammatory disease of the fibromuscular tissue influences the superimposed protective columnar or squamous cells, producing in these either hyperfunction or hyperplasia, or both, and, if the process is more destructive, we find a loss of these protective surface epithelia and the initiation of erosions. Long-continued inflammatory irritation may at any time change controlled hyperplasia into uncontrolled invasion which spells cancer.

To understand the pathology of inflammatory diseases of the cervix and the consequences which follow from these, one must know the minute histology and physiology of this organ.

HISTOLOGY AND PHYSIOLOGY OF THE CERVIX

Unlike the uterus, the cervix has no highly specialized intermediate cellular structure such as that in which the endometrial glands are

always imbedded. The racemose, deeply burrowing, cervical glands are imbedded in common clay, an ordinary fibromuscular tissue, differing in no particular manner from similar structures in other parts of the body. This fibromuscular tissue has several functions to perform. It acts as a nucleus into which the supporting tissues of the pelvic floor find an anchorage, thereby allowing freedom of movement to the superimposed uterine body. Movement to this portion is essential to the proper performance of its highest function. Second, the cervical fibromuscular tissues act as a sphincter to the uterine contents. To permit wide dilatation of this sphincter without undue destruction, the muscular element must greatly outweigh the fibrous element, thereby permitting of an elasticity which would be otherwise impossible. This normal proportion of muscular (sphincteric) and fibrous (supportive) tissues is frequently altered, always to the detriment of the muscular element, by errors in development, abnormal puerperiums, infection, newgrowths and age.

Musculofibrous tissue of the cervix differs in its pathology in no particular sense from similar tissues elsewhere in the body, except owing to the presence of two factors: the influences brought to bear by being invaded by glands, and the influences of the functional phases associated with procreation.

The glands of the cervix are a protective mechanism; they are constituted by digitations of a common duct lined by a single layer of tall columnar cells. These are mucous goblet cells, in which normally the tall cell has a nucleus near the base and an open end toward the lumen, like the cup of a tulip. Below these is a layer of flattened cells constituting the so-called basement membrane. Normally, the quantity of secretion is just sufficient to fill the cervix with a tenacious stringy plug which protects the uterine cavity from invasion. It flows slowly like a glacier. This plug liquefies, when in contact with the acid secretion of the vagina, and acts further as a lubricant to this canal. The reason for the digitations of the cervical glands is found in the desire to increase the extent of functioning surface and thereby lessen the function of each individual cell. It is a maximum of function with a minimum of exposed surface. Unlike the endometrium, the cervical tissue has a permanency which may act to its own detriment. The uterine mucosa, by shedding its surface, also sheds many of its diseases, as will be pointed out in another paper by me. The cervix retains the scars which it cannot heal by the ordinary corporeal reparative processes. The processes associated with procreation come but slightly, if at all, to its aid. The cervix undergoes slightly transitional changes with menstruation, and marked hypertrophy, increased vascularity and glandular function during pregnancy, with regression during the normal puerperium, but it has not the happy faculty of casting off the scars of this maelstrom

of cellular disturbance. It must depend upon the general recuperative properties of the body as a whole for its reversio ad integrum. The tissues of the genital tract suffer from a state of unrest, a flow and ebb, that may affect other parts of the body, but to a much less degree. This state of flux may operate to the advantage, or disadvantage, of the affected tissues. But it is often productive of pathologic states, or it may greatly modify these when they are present.

Inflammatory changes of the cervix may be simple or special, acute or chronic, or they may spend themselves chiefly upon the cervical glandular structures affecting the fibromuscular layers minimally, or they may affect these component tissues in the reverse order.

General.—Most inflammatory cervical diseases begin as an acute process and degenerate into chronic catarrhal states. Others are acute and short-lived. It is characteristic of acute mucous membrane diseases that, when they end abruptly, they leave a minimum of change in tissue or function. Chronic inflammatory disease, on the other hand, is productive or destructive, according to its intensity relative to the body reactions. Productive inflammatory diseases, that is, the more chronic processes, express their production in either hyperfunction or hyperplasia. The destructive types produce loss of tissue, expressed as erosions or ulcerations.

There are other functions which initiate productive changes in the cervix, essentially causing enlargement of the fibromuscular tissues, chiefly with minor incidental, or major accidental, changes in the endocervical epithelium. These are the cervical hypertrophies of pregnancy without normal retrogressive changes in the puerperium, leaving a permanently enlarged cervix usually associated with cystic disease. Other productive cervical diseases may arise out of the stimulus of corporeal fibroids. These, of course, simulate a pregnancy, causing hyperplasia of all the tissues as in pregnancy. After all, fibroids are the barren woman's children. When the uterus has prepared the functional endometrial and allied changes repeatedly without issue, fibroids develop as a pseudopregnancy. The influence upon the cervix is frequently quite similar. Such hypertrophic changes when not followed by retrogression, as in the normal puerperium, result eventually in a large, hard cervix, which, when associated with cystic disease, may assume large proportions. Since this is most commonly the aftermath of an abnormal puerperium, the cause, or causes which inhibited the reduction usually also affect the uterus, causing it to remain in a state of chronic subinvolution, thereby remaining globular, tender, large, superimposed upon a cervix similarly affected. In fact, the condition of the cervix is being recognized more and more as the index of the state of the uterus, and this applies as much to the mucosal as to the fibromuscular changes. Such conditions of the cervix should be distinguished by the name of "chronic interstitial

anterior lobe. It appeared necessary to administer large hormonal doses in order to regulate the function of the anterior lobe.*

I injected amenorrheic women with the quantities of hormones necessary to induce menstruation, i.e., 200,000 to 300,000 M. U. dimenformon during a period of twenty days, and 5 Rab. U. of progesteron daily during the following 5 days.

In the first case thus treated, the result was negative, i.e., the increased excretion of prolan A remained uninfluenced. I reported briefly on this fact in my book.⁸ On continuing these studies I found that the regulation of prolan A elimination is different in proportion to the degree of ovarian dysfunction. In cases where the ovarian function has not yet ceased entirely, i.e., where menstruation had disappeared for a few years only, one may succeed in reducing the excretion of prolan A. In both cases of secondary amenorrhea, it was possible to reduce excretion of prolan A by a sufficient dose of follicular hormone. Before the beginning of the bleeding (pseudomenstruation), excretion of prolan A had already been influenced. In the second case, though we did not succeed in inducing any bleeding, the prolan A content of the urine was decreased.

The conditions are somewhat different in primary amenorrhea and castration, i.e., in cases where ovaries had never been functioning or the sexual glands had been removed. In Case 3 real menstrual bleeding had been induced by means of dimenformon and progesteron, but elimination of prolan A could not be decreased. Also in Case 4 the hormonal provocation of menstruation could not influence the elimination of prolan A. Only after the second treatment did we succeed in lowering the prolan A level in the urine. The castrated woman was treated with hormones for several months, and we regularly succeeded in inducing pseudomenstruation or menstruation, respectively, according to the method of treatment. But we did not succeed in influencing the increased excretion of prolan A.†

SUMMARY

1. The loss of ovarian function is characterized by an increased excretion of follicular hormone in the urine (more than 111 M. U. of prolan A per liter). The increased excretion is probably caused by hyperfunction of the anterior lobe of the pituitary in the absence of any inhibitory action of the ovary on the anterior lobe.

*The periodic ovarian cycle may, as I reported a short time ago, (Wien. klin. Wchnschr. 15: 455, 1936) be influenced by follicular hormone. If 100,000 M. U. dimenformon are injected into a woman of the procreative age during the sixth to twenty-fifth day of her cycle, menstruation fails to appear. That means that we have induced an artificial amenorrhea.

†In the meantime R. T. Frank and U. J. Salmon (Proc. Soc. Exper. Biol. & Med. 33: 311, 1935) succeeded in temporarily ameliorating the hypophyseal hyperactivity in 14 various cases of menopause. The authors injected from 4,000 to 22,000 R. U. estrogenic factor (divided in doses of 4,000 R. U. at intervals of 2 or 3 days) and observed a rapid decrease of gonadotropic factor in the blood and urine. The disappearance of the prepituitary hormone persisted for from 28 to 70 days but was regularly followed by a return to the condition of excretion noted before treatment.

Chronic Endocervicitis.—The picture of chronic endocervical disease from a microscopic standpoint varies greatly with its intensity and duration. In the mildest form there is merely increased activity of the surface columnar epithelium; chiefly that part nearest the cervical canal is most profoundly affected. The deeper one recedes from the canal into the digitations of the glands, the more normal the columnar cells become. This is quite the commonest picture.

The Hypersecretive Types of Endocervicitis.—If we examine the columnar cells more closely near the canal, we find that the goblet part of the cell, that is, its free margin, is more ragged, and is expelling huge quantities of mucus (Fig. 1). The nucleus has moved away somewhat from the base of the cell, and may occasionally ascend as far as the middle, leaving a clear space underneath it. Tinctorially the nucleus does not stain so deeply. A drop of this cervical secretion, pressed between a slide and cover slip, shows a most impressive



Fig. 1.—Showing to the right marked hyperfunction of the columnar cells, with desquamation of the cells by a sort of explosive excess of function.

picture of thousands of mucous masses shaped either as clubs, sausages, or ovoids, lying in a stream of thinner matrix, with their long axis in the stream line. Each globule has a surface of higher tension which causes it to retain its shape until this is dissolved. These globules are highly granular, and are very beautiful and highly refractile. They may be easily mistaken for the highly refractile encysted types of trichomonas. But their arrangement in streamline fashion at once affords a differentiation. In the more advanced and more intense chronic infections, this state of hyperfunction expressed as hypersecretion may cause a complete explosion of the secreting (Fig. 1) cells, with or without attempts at repair in the deepest basal (Fig. 2) membrane. In still other more acute stages, a wholesale blight may affect all the columnar cells, causing them to be cast off in a state of partial disintegration, not only of the surface, but of all the deeper glands. Secretion is not a prominent feature of this stage, rather destruction captures the attention.

cervicitis," as contrasted with purely catarrhal endocervicitis, in which the disease is restricted wholly, or chiefly, to the glandular structures.

Acute Catarrhal Endocervicitis.—Acute catarrhal endocervicitis may arise from any acute infection of the cervical glandular surface. It may occur independently of pregnancy or as a result of the traumatism of labor. The common agents of acute and chronic disease are the gonococcus, the streptococcus and the long-continued irritation of trichomonas with its associated symbiotic organisms. The former is, in the vast majority of instances, merely a surface and subsurface infection, producing hyperfunction and cystic degeneration, owing to duct constriction and round-celled infiltration. The secretions are usually purulent, but may later be merely superabundant or even show no appreciable departure from the normal. The postpartum cervical changes incident to an acute infection were described by me* where a streptococcal film is frequently seen over the cervix in the early days following delivery. As chronic endocervicitis is the common sequela of an abnormal puerperium, a few lines devoted to the subject may be enlightening.

It is variously estimated that from 50 to 70 per cent of women show a chronic endocervicitis following pregnancy. I was one of the first to draw the attention of the medical profession to this abnormality. It is not surprising that it is so frequent. The condition of the cervix and its mucosa immediately after labor, especially after first labors, cannot but cause one to respect the great recuperative power of damaged tissues in the puerperal state. When one sees the ecchymotic endocervix, torn from its moorings, frequently hanging like a veil, bloody, bruised, and lacerated, and the fibromuscular tissues torn, divulsed, gray and necrotic by counterpressure from pelvic bony structures against the presenting part, we repeat, one is struck with admiration at the recuperative power of the puerperal woman. A repeated examination five or six weeks later, in a large number of cases, shows the miracle. But the miracle is seldom complete. The fibromuscular structures, like all mesoblastic tissues of the body, have a larger recuperative power than a more highly specialized tissue. Consequently, the glandular tissues suffer more and recover less of their high specialization. Columnar surfaces are the great weakness of the body. It is from these that most diseases find their portal of entry, or local permanency, so that local infections of their surfaces have a faculty of becoming chronic, irritative and vitiative of normal functions.

The diseases of the nasal mucous membrane bear a close resemblance to those of the cervix uteri.

*AMERICAN JOURNAL OF OBSTETRICS & GYNECOLOGY 16: 339, 1928.

fibrous tissue minimally. Hyperplasia of the glandular elements results in a many layered covering, instead of a single layer (Fig. 3). In many instances, this gives rise to a heaping up of tissue in which secretory function is partially, or totally, lost and cell energy seems to spend itself chiefly in division. These can so closely approach a cancerous stage as to qualify as precancerous, a vague term without justification. The cell division may affect either the columnar cells or the squamous covering. These two types of cells may so revert to their embryonic characters as to be indistinguishable. The columnar cells lose their columnar mucus-secreting characteristics, and the squamous cells cease to be keratinized, become active, and the surface cells are shed before they can become adult as in the normal state. The underlying fibromuscular stroma is usually but slightly affected by the mild infection.

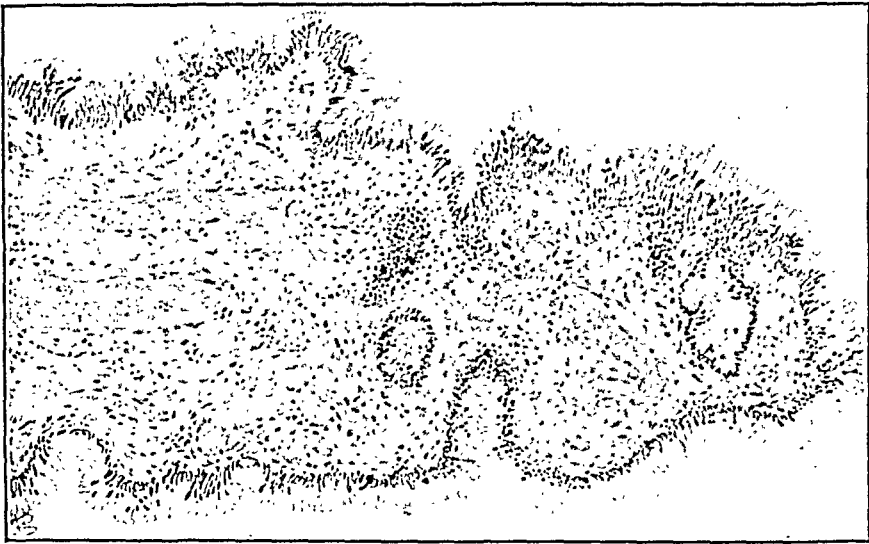


Fig. 4.—A polyp of cervical canal, showing catarrhal changes in the columnar covering cells, edema of the fibrous core and multiplication of blood vessels, a vascular edematous polyp in which both supporting and special cells are involved in a vascular hyperplasia.

Acute Interstitial Cervicitis.—It will be readily understood that the division of cervical diseases into catarrhal and interstitial, and into acute and chronic types, is a purely arbitrary one for descriptive purposes. These types pass insensibly from the one into the other. But the division is one that is generally accepted for similar disease processes in other parts of the body.

Where the inflammatory attack spends itself upon both the lining and the deeper tissues (predominantly postpartum cases) in addition to the mucosal changes, described above, one finds diffuse round-celled infiltration of the deep tissues, with the development of large cervical polyps (Fig. 4), frequently much pendunculated, with an infected, desquamated surface at certain points, and a loose edematous fibrous core. Thrombophlebitic changes are frequent and conse-

Hyperplastic Type of Catarrhal Endocervicitis.—In other cases, hyperplasia of the glandular linings becomes the predominant feature. This may spend itself chiefly upon the glandular elements affecting the

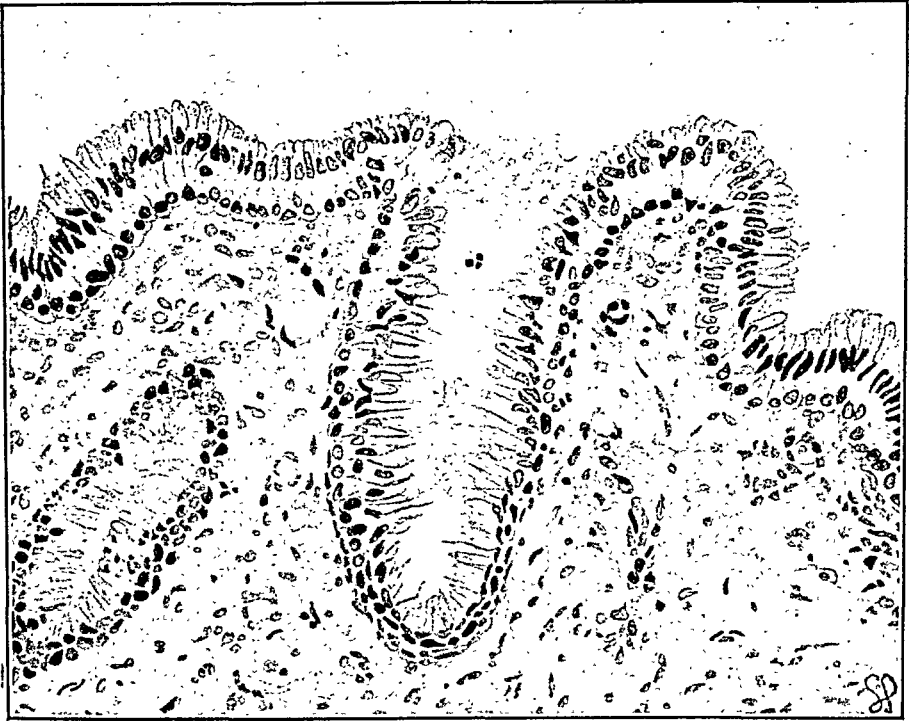


Fig. 2.—Catarrhal endocervicitis. Note the duplication of columnar lining. The more superficial layer is being desquamated by the deeper layer under the stimulation of disease. The underlying tissues are edematous.

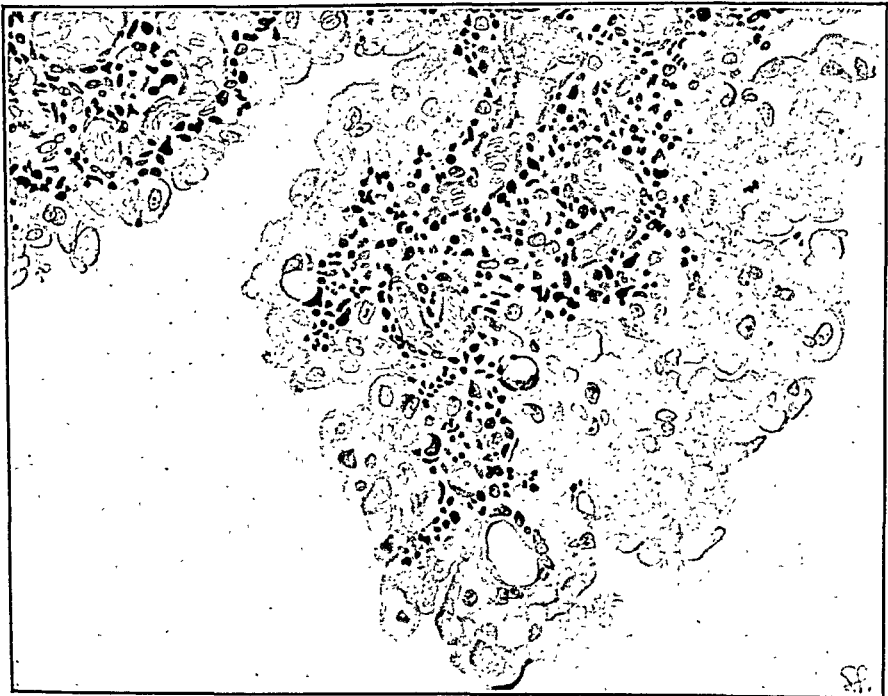


Fig. 3.—Subacute inflammation of the endocervical tissue. There is round-celled infiltration, great vascularity and inordinate multiplication of the columnar cells that are often multinucleated and syncytial in character.

as a consequence of secretory pressure. When the intracystic pressure equals the cellular secretory pressure, then secretion ceases and regressive atrophic changes occur in the lining epithelium, causing all degrees of flattening and frequently complete atrophy of the lining cells. The contents of the cysts may vary from thick tenacious mucus at first, later, purulent, or inspissated white mucus, or liquid clear contents. These different results are the consequence either of the type of infection, or of the duration of the cysts.

There is one feature of this cystic disease that has not been realized. This is the frequency with which the cervical glands at the internal os are affected. Cystic degeneration of the glands at, or near, the external os are visible and therefore frequently described, but cystic disease of the internal os with partial occlusion of the canal and imperfect drainage are very frequent occurrences, in fact, almost as common as the discreet type, but of infinitely more interest because these can arise from both an ascending or a descending infection. The great frequency of old cystic disease of the internal os has another interest. In a descending infection of tubercular origin there are certain points of predilection or sedimentation where the disease metastasizes. Notably one of these is the region of the internal os. Perhaps it is imperfect drainage which determines this. Doubtless there is always delay at any constriction and the internal os is a very decided constriction of the uterine cavity, and, where stasis occurs, circumstances favorable to deranged function and infection must follow. Cystic disease of the internal os, now recognized as a very common condition, has a profound effect upon treatment which will be dealt with at a later period.

Ectropion.—Ectropion, commonly described as erosion, cervical ulcers, et cetera, is a reddened area about the external os, usually concentric with it, varying in size from a small area the size of a five-cent piece to an extension that may involve the whole portio. Although mostly concentric with the external os, it may involve chiefly the anterior lip in an anteverted, or the posterior lip in a retroverted and retroflexed uterus. These differences of spread are accountable to degrees of vascularity. The origin of ectropion is interesting. It can never exist without antecedent endocervicitis from which it springs, and it cannot be cured without first or simultaneously curing the endocervicitis. Endocervicitis is primarily an infection, usually a chronic one ab initio, or degenerating into a chronic state from an acute one. Infection determines blood to the part, which, if prolonged, leads to the development of new capillaries. This congestion leads to certain defects of function, which expresses itself in hyperfunction (leucorrhea) or hyperplasia (division) or both. Hyperplasia does not necessarily have to be accompanied by hyperfunction, so that grave states of endocervicitis may be devoid of signs of leucorrhea. When congestion

quent diapedesis or large venous hemorrhages may occur, not infrequently followed by sloughing. Cystic disease of the glands usually occurs only in the chronic state.

Chronic Interstitial Cervicitis.—This is usually the result of an infection following full-term labor or abortion. The characteristic clini-



Fig. 5.—Showing eroded surface and multiple cystic disease of the cervical glands, with pressure degeneration of the lining cells. This is at the external os.

cal signs are an inordinately large cervix, the result of chronic subinvolution, with numerous nabothian cysts, which greatly add to its bulk (Fig. 5).

Owing to the hyperplasia of connective tissue and the frequent collections of lymphocytes resembling lymph nodes developed, we think, from the reticular tissue lining the lymph spaces, fibrous constriction of the ducts of the racemose glands occurs, and retention cysts occur

which open onto the squamous portion. This is for protection of the more delicate columnar lining. Third, there is no definite line where columnar lining ceases in the region of the external os. It varies in the height it may invade the cervical canal in different individuals. Fourth, columnar epithelium never replaces squamous epithelium where the underlying soil is hostile to the more hardy

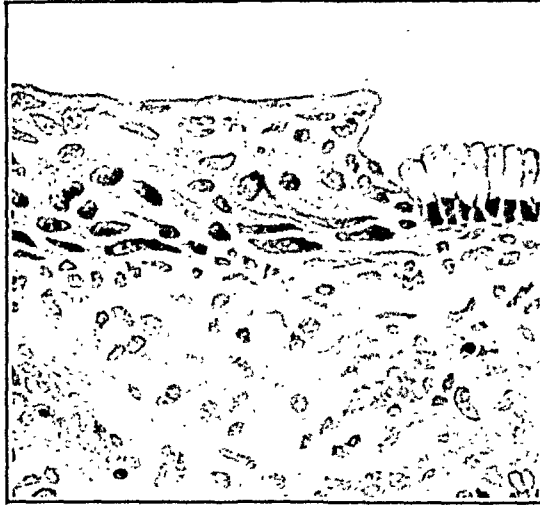


Fig. 6.—Normally the transition from squamous to columnar cells is abrupt.



Fig. 7.—Where cervical glands open on the portio, the more hardy squamous lining dips into the mouths of the glands to protect the more delicate, highly specialized columnar lining.

squamous covering. Where squamous cells cannot survive, it is not possible that a more delicate columnar cell could accommodate itself. Under certain circumstances of change, linear arrangement of the basal layer of a squamous covering may simulate that of columnar cells which are undergoing hyperplasia. But this cannot be interpreted, by any stretch of the imagination, into an interpretation of a replacement of squamous by columnar cells. We repeat, such a con-

has gone on for a considerable period, it leads to hypernutrition or deranged nutrition. The changes described above under chronic endocervicitis now develop. It is only a matter of time before the squamous epithelium, covering the portio, begins to feel the effects of this congestion, and the part that will feel it most forcefully will be the tissue in the immediate neighborhood of the canal, namely, the external os. The basal layer of the squamous epithelium here begins to multiply under the stimulus of hypernutrition. As the division is speeded up, the cells have not time to become adult, imbricated and keratinized before they are pushed off by the press of new cells. The result is a reddened area made up of granulation tissue composed of embryonic squamous cells. This process gradually, but very slowly, extends to give rise to an increasing area of ectropion. If one examines such a section microscopically, beginning from a normal portion of the cervix and thence gradually approaching the region of the internal os, one finds the squamous layer gradually losing its thick keratin layers, and the whole covering growing thinner until at the margin of the ectropion there remain only the basal layers, arranged as deeply staining vertical cells with a layer or two of embryonic cells covering these. Further on, only a single layer remains, and, still further, even this disappears, leaving only occasional islands of cells of squamous origin on a granulating, small-celled infiltrated surface. Islands of highly modified squamous cells may still be found here and there, especially in the neck of the glands which open onto the surface. It is from these that recovery takes place when effective treatment has been applied.

It may be stated with assurance that the common teaching that under inflammatory stress columnar covering may replace squamous epithelium over an area of ectropion is not only wrong theoretically, but also wrong in our experience. Our specimens were taken entirely from the total hysterectomies at operation. The vagina was washed out with a gloved hand only, and liquid green soap. Immediately after the operation the uterus was opened lengthwise, examined, recorded, and a strip about $\frac{1}{3}$ cm. thick was then taken from the fundus to the portio, and immersed immediately in bichromate of mercury in formalin. In the majority of cases this strip was cut in one section. If too long for section, it was cut across above the internal os and its continuity was maintained on two slides instead of one. Under these most favorable conditions, where tissue was not more than one hour out of the body before being hardened in its easily penetrated strips, it can be definitely stated that normally squamous cells end abruptly where columnar begin. The transition is from one definite type to the other in a clear-cut line (Fig. 6). In the normal there is no room for any doubt on this point. Second, squamous lining normally dips down into the gullets of those cervical glands

newal at each menstrual phase. The upward extension of chronic endocervicitis is limited to the deep layers of the uterine mucosa.

CAUSATIVE AGENTS

There are immediate and contributing agents. The immediate agents are of course microbic. These are chiefly streptococcic, but also gonococcic, trichomonas symbiosis, and rarely of other types. Contributing factors are of the greatest importance. Of highest frequency, of course, are the results of full-term labors and septic abortions. In the former, the traumatic and disruptive influences are the agents which supply the favorable soil. But defective drainage during the recovery stage lends an additional disadvantage. When a woman lies supine, the vagina drains uphill at an angle of about 35 degrees. As a consequence, the traumatized cervical mucosa lies in a cesspool of lochia, from which, after forty-eight hours postpartum, many strains of microorganisms can be cultivated. Each succeeding pregnancy adds its quota to the initial invasion. Carcinoma of the cervix is a rarissima avis in the nullipara. It is a disease restricted to the parous woman. One might almost say, uniformly so. The cause lies not in accidental tears of the cervix, but in the irritation of a chronic endocervicitis or its consequent ectropion. Tears of the cervix play no part in this process, except as a contributory factor in exposing the delicate cervical mucosa to traumatism, or in making it more easily accessible to infection. A great deal too much importance has been attributed by clinicians to cervical tears. Their repair is a matter for profoundest consideration, not only as regards the dangers, but also owing to the almost complete futility of the operations that are commonly used for this purpose. Another contributory cause is found in that type of individual whose mucous membranes are all susceptible to overgrowth, tonsils, adenoids, intestinal and endometrial. By heredity, or acquisition, they are prone to develop disease of the mucous membranes. Other chronic diseases which lower the general resistance may be strong contributing factors in the development of cervical disease.

SYMPTOMS AND SIGNS

The symptoms of endocervicitis are local, extensive and general.

In the nonpuerperal state, acute endocervicitis produces at first leucorrhea, copious and purulent. Later, there frequently develops a feeling of weight in the pelvis. Menstruation may be retarded and then prolonged and profuse. How much of these last symptoms may be due to involvement of the endometrium and appendages, which may develop by extension, it is impossible to tell. Pain, in uncomplicated inflammatory cervical disease, is conspicuously absent. Extension frequently takes place to the endometrium, which is not diagnosable until the appendages are reached. Pain now becomes a conspicuous

tention is not only illogical, but contrary to experience. Wherever there is much surface contact with externals, nature interposes squamous epithelium as the safest guard, and the transition from squamous to columnar surfaces is proportionate in degree to the diminution of these contacts. This is a general rule of physiology. Columnar surfaces, and transitional epithelia, on the other hand, under the influence of irritation and frequent contacts, can become hardened and stratified to resemble a squamous covering, but serration and other features are generally absent. The cervical canal and the distribution of its cellular elements will repay a consideration. The canal varies considerably in shape and size under varying circumstances. Normally, it is fusiform, small at top and bottom with a slightly wider center transversely to the body. The anterior and posterior walls lie in contact, each with its frondlike arborvitae arrangements of its folds which by their inclination favor downward drainage. The glandular elements penetrate more deeply into the substratum and are more numerous near the external os. A few open onto the portio. Glandular elements grow less penetrating and with fewer digitations, the nearer one approaches the internal os. The glands are set in adult fibromuscular tissue. One does not encounter the specific interstitial cells of the endometrium until well beyond the internal os, and as soon as one meets these cells, the imbedded glands change immediately into specific uterine tubules.

The depth of tissue involved in glandular invasion at the internal os is singularly thin, and, in abnormal states, is frequently cystic. One can readily see how easily the region of the internal os can be injured and cicatrized by inflammation or traumatism, where glandular recuperative power must be slight where it is so scant.

Under inflammatory disease the canal gradually widens. In nulliparae and virgins this widening involves chiefly the middle portion. The internal and external orifices are more resistant, owing to their greater protection by the uterus above, and by the squamous covering below. The result is a craterlike enlargement of the canal with stasis of secretion or blood. At postmenstrual periods stasis increases the effect of infection. Eventually the periphery of the external os becomes secondarily involved in ectropion and the os widens spontaneously. Presumably similar changes take place at the internal os. It is common experience to find both the external and the internal ora open widely when one cauterizes nulliparas or virgins where prolonged cervical disease has been present. That the cervical disease eventually invades the endometrium by extension upward, we have abundant proof, which will be reserved for another work. That it produces ectropion by extension downward admits of easy demonstration. The surface layers of the endometrium, however, remain immune to this upward extension, owing to their desquamation and re-

2. An attempt was made to influence the increased prolan excretion by inducing pseudomenstruation or menstruation. This is successful in proportion to the severity of the ovarian dysfunction.

If the functional inhibition of the ovaries exists a few years only (secondary amenorrhea), elimination of prolan A can be decreased by administering the quantity of follicular hormone required for inducing pseudomenstruation.

If ovarian function has never been present (primary amenorrhea), even the induction of menstruation may not depress excessive elimination of prolan A. This is only possible after repeated induction of menstruation.

In the castrated woman, prolan A production will not be influenced even if pseudomenstruation or menstruation, respectively, could be induced for several months in succession.

3. The disturbance of the gonadotropic function of the anterior pituitary is not of the same kind in primary as in secondary amenorrhea. This is shown by the fact, that excessive production of gonadotropic hormones may be influenced by means of ovarian hormones in cases of secondary amenorrhea, but they are scarcely or not at all to be influenced in cases of primary amenorrhea.

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Young, James: *Birth Control, Contraception and the So-Called Safe Period*, *Brit. M. J.* 1: 1091, 1936.

A steady decline in birth rate of most western communities during the past sixty years is ascribed in the main to the operation of intentional restriction of fertility. The author discusses three ways in which such restrictions are attained—abstinence, abortion, and contraception.

The safe period as formulated by Ogino-Knaus is described and criticism of it offered. From the practical standpoint it may be summarized that there exists evidence to suggest that if certain criteria are rigidly observed birth control based on the safe period can be employed with a reasonable measure of certainty. Where any variation in type exists, the difference in days between the minimum and maximum cycles is added to the beginning of the fertile period as based upon the maximum cycle. Adjustments may be required after childbirth, abortion, debilitating diseases or any drastic alteration in the routine ways of life.

Mechanical contraceptive methods are briefly outlined. The vaginal check pessary is recommended.

Birth control must be accepted by the profession as a procedure which comes within the purview of medical practice.

F. L. ADAIR AND S. A. PEARL.

symptom. Local or general peritonitis of a mild or severe degree follows. Every acute case tends to become chronic in time. Occasionally spontaneous cure follows immediately upon the acute stage. General symptoms of malaise, backache, loss of appetite, indicative of a toxemic state may or may not follow. Occasionally, though fortunately rarely, general blood infection, without appreciable involvement of the pelvic organs other than the cervix, may develop, causing a general septicemia without localization, or multiple involvement of synovials, endocardial, pleural, meningeal and lymphatic. Pyemia is rare.

In the acute puerperal state there are all degrees of activity. In the majority, the disease remains a local involvement of the cervical mucosa and its lacerations. There are no distinguishable symptoms in the early days of the puerperium. The appearance of the cervix after the third day, described in a previous article and lecture before the Philadelphia Obstetrical Society, shows an edematous state, frequently with a film, a streptococcal membrane over the visible part of the cervical canal. This may be easily wiped off. Symptomatically, however, one finds that the puerperal temperature does not remain normal. There is a daily rise to 99° or 100° F., over many days, with a total absence of pain. This is indistinguishable from a low grade pyelitis, or an inconspicuous pelvic thrombophlebitis. Forty per cent of cases of pyelitis are pain-free. Pelvic thrombophlebitis may be suspected but cannot be diagnosed, except by its mechanical complications. So the mildly febrile pain-free cases in the puerperium may be either acute endocervicitis, pyelitis, or thrombophlebitis. In about 90 per cent of cases the correct diagnosis will be endocervicitis. It is not advisable to expose the cervix and confirm the diagnosis. The cervix is retarded in its involution, as is also the superimposed uterus. This applies equally to the ligamentous structures. Extension of cervical disease may be by continuity of mucous membrane, or by the lymphatic channels. In the former type, pain due to peritoneal involvement is frequently late in development, often involving weeks, with the interval of only comparative well-being. May we outline a recent case the better to illustrate this important, and all too frequent sequela of labor?

I was called in consultation to see a case which had been delivered in hospital one month previously. Her labor and puerperium had been clinically absolutely normal, and symptom-free. She went home on the twelfth day. Ten days later, she had a severe pain in the pelvis, midline, which subsided after one-half hour. Two days later a similar attack developed. This was repeated two days later, but it did not subside this time. Her doctor sent her back to hospital. When I saw her, she had an acute abdomen limited to the lower half, with exquisite tenderness especially over the right side. Naturally, owing to the recent labor, one thought of pelvic complications. Vaginally and rectally nothing but a fullness in the pelvis with great tenderness on imparting movement was elicited. Leucocytes 22,000. There had been nausea and vomiting in the last six hours. Appendicitis could not be ex-

cluded, but pelvic peritonitis was suspected. The abdomen was opened along the right rectus. The appendix was free in its proximal two-thirds, but was involved secondarily between two swollen, indurated tubes, curved each about its ovary. The appendix was liberated and removed and the abdomen closed. The patient made an uninterrupted recovery. There was absolutely no history of gonococcal infection.

It is now becoming more and more recognized that such ascending infections of a mild streptococcal nature are exceedingly common. They are insidious and slow in development. They have been of frequent occurrence in my experience. Smears showed only streptococci. Most of these are mistaken for gonococcal disease. They run a similar, but milder course usually. Sterility may follow, but not so consistently as in gonococcal disease. In the cases where the endocervicitis spreads by lymphatic extension, the first sign of involvement of the peritoneum usually comes on during the early puerperium. A sudden severe state of pain in one or the other lower quadrant, more frequently the left, usually leaves no diagnostic doubt. There is tenderness and a sudden rise of temperature which subsides under appropriate treatment.

Examination, both bimanually and by exposure of the cervix, of all puerperal cases five to eight weeks postpartum, should be a routine. Under these circumstances endocervicitis will reveal itself by a prolonged lochia, followed by a copious leucorrheal discharge, probably a degree of subinvolution of both cervix and uterus, very likely tender uterosacrals and backache. On exposure the cervical mucosa secretes a tenacious clear or semipurulent plug. The canal is more patulous than normal and the mucosa has an unhealthy edematous, pale red appearance. In the chronic state, which is by far the most common type that one sees, the patient usually complains of a leucorrhea of long standing, but growing progressively worse. In young girls and nulliparas, this may be the only symptom. On examination there is a velvety feel about the os which is characteristic of ectropion. When this is present the external os assumes proportions of patulousness that are unusual in nulliparas. When the condition has not reached the stage of ectropion, one frequently finds the external os closed, but, on opening it with a forceps, a great quantity of tenacious mucus from a largely dilated, craterlike canal is obtained.

The ectropion, when present, may be slight or extensive, but rarely exceeds a ten-cent piece in size, in these cases. It is red, granular, and bleeds when cleansed.

In multiparas the process is usually much more extensive. Each pregnancy and labor adds its quota of exacerbation. The leucorrhea becomes more abundant and more troublesome during pregnancy. The patient may complain of backache, fatigue, and poor health. That

poor states of health may be due to this "cervical tonsil" is confirmed by the great improvement which follows upon effective treatment of this condition.

There are two types that are easily distinguished. In the first, the disease is confined almost exclusively to the involved mucous membrane and its ectropion, *chronic catarrhal endocervicitis*. In the second

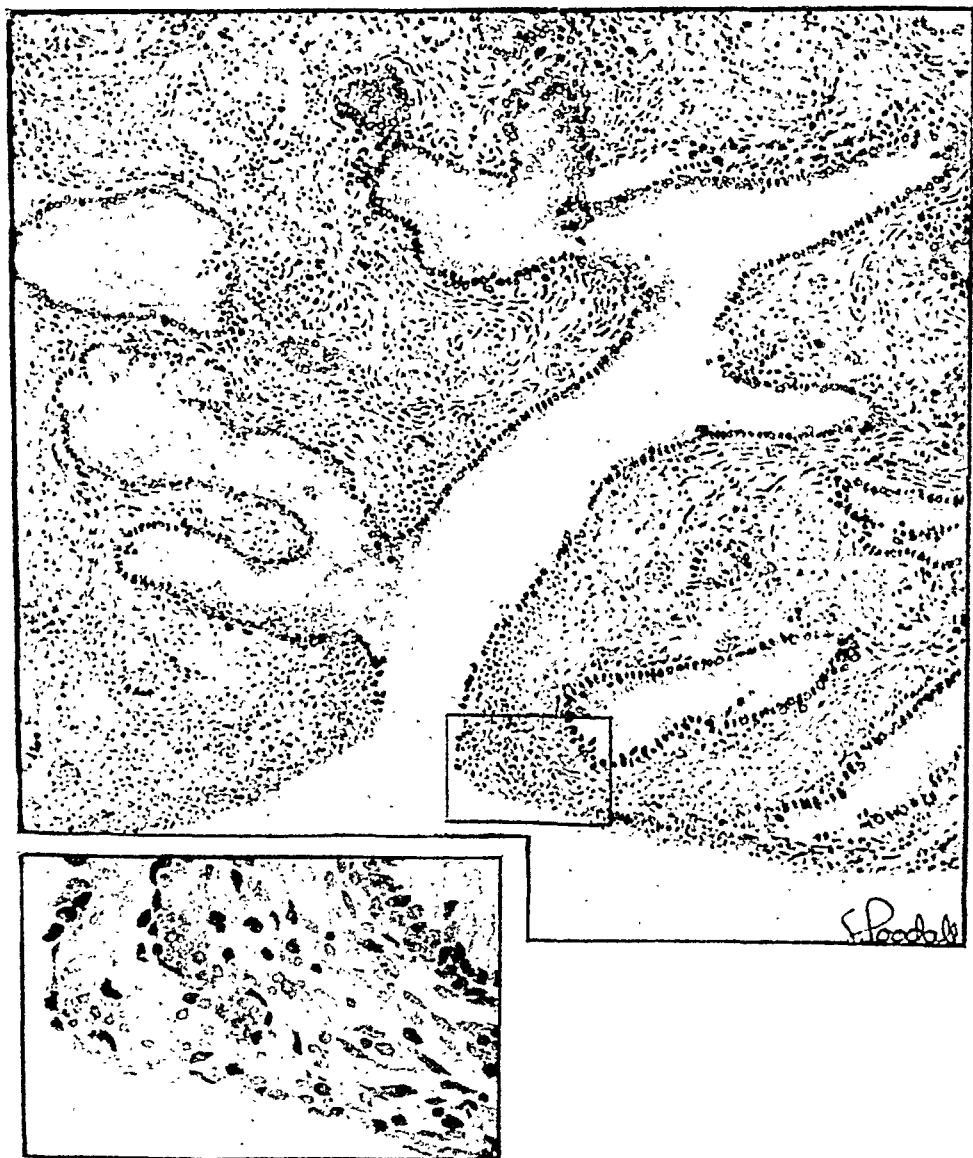


Fig. 8.—A, Surface erosion of the edematous, hemorrhagic type without much round-celled or leucocytic infiltration. B, The same magnified; note absence of covering columnar epithelium and great vascularity.

type, the cervix as a whole is involved, *chronic interstitial cervicitis*. This distinction is of paramount importance. There are intermediate cases, but generally speaking, they fall conveniently into these two big groups.

Endocervicitis with Ectropion in Nulliparas.—The cervix is more patulous than normal. There is a copious, clear, tenacious discharge;

occasionally this is white with mucous corpuscles, or even semipurulent. The mucous membrane of the canal is occasionally pale and edematous, or red and granular; sessile or pedunculated polyps may fill the visible portion of the os (Fig. 8). The area of ectropion may be extensive, usually concentric; granular and bleeding points are frequent when the surface is cleaned. Frequently a large vessel will emerge from the granular ectropion and course outwardly to the periphery. These sometimes assume large proportions. At other times the outer margin of the ectropic area presents one of two characteristic pictures. In the one, there is a blueness at the periphery as if there were venous congestion below the thin squamous margin. In the other, there is a white rim of heaped-up epithelium surrounding the ectropion as if sugar-coating had been applied. These differences arise out of differences of congestion and lack of balanced desquamation.

When the cervical canal is invaded for treatment, its irregularities, owing to enlargement and sessile overgrowth, become apparent, and dilatation of the internal os is frequently so wide as to give the impression of passing insensibly into the uterine cavity without definable limit to the canal.

These findings of irregularity in the cervical canal, owing to overgrowth of epithelium, may vary greatly in degree. In many cases the endocervical infection will spend itself chiefly in hyperfunction expressed in an abundant discharge. The difference is one inherent in infection and local resistance.

Chronic Cervicitis.—This is a disease of the parous woman. It is a sequence of an abnormal puerperium, whether full term or post-abortum. The distinguishing features of this disease lie in the large dimensions of the cervix, its hardness and its associated cystic involvement. It is a disease of multiparas, in which, owing to involvement of all the cervical tissues in infection, or owing to some general debilitating cause or causes, the normal involution of the cervix has been incomplete. The dimensions vary considerably from a slight enlargement to proportions that fill the vault. Hardness is a characteristic. Nabothian cysts are the rule and frequently stand out as sagolike bodies over the portio. The cervical canal is tortuous, granular, and hard. Everything seems fibrous. The uterine body is similarly involved in a state of chronic subinvolution, as evidenced by a large globular symmetrical, usually tender corpus. This condition is frequently described in textbooks as "chronic metritis," "chronic fibrosis uteri" and "arteriosclerotic uterus." Endocervicitis and ectropion usually accompany the cervicitis but these may not be prominent.

It is most important to distinguish the cases that are dominantly endocervical from those that are dominantly cervical, because the treatment is essentially different.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of inflammatory diseases of the cervix from other conditions lies essentially between advanced cases of chronic inflammatory disease and incipient carcinoma. We know of no rule, except clinical experience and biopsy.

The insidiousness of the change from inflammatory disease to new-growth cannot be better illustrated than in the records of St. Mary's, where, in the pursuit of this work, two cases of unsuspected carcinoma of the cervix were found in the microscopic study of uteri removed by total hysterectomy by the authors, in the past year, roughly, somewhat over 2 per cent was found in 90 cases. Two others were placed in the category of precancerous hyperplasia, a rather loose term to designate overgrowth with solid masses filling the acini, but no evidences of breaking through the normal external glandular boundaries.

TREATMENT

The whole of this treatise has for its object a plan to outline a *logical* treatment of inflammatory cervical diseases. The conclusions that are about to be expressed are based upon a studious knowledge of pathology and a wide clinical experience. It is an expression of very firm convictions.

The subject may be dealt with most convincingly under three headings.

1. Nonsurgical treatment.
2. Surgical treatment.
3. The influence of a residual inflammatory cervical disease upon pelvic operations.

1. *Nonsurgical Treatment.*—There are very few forms of treatment of the inflamed cervix that offer any hope of recovery or even amelioration other than the thermocautery. Prior to its introduction, the medical profession leaned strongly to preparations of tincture of iodine, carbolic acid and other escharotics. Later, diathermia and "Elliot" enjoyed a vogue. These have been abandoned for the more rapid, more controllable and more effective electric thermocautery.

It is chiefly to the efficacy and limitations of this presently universal treatment that we wish to draw particular attention. Thermocautery is a very effective form of treatment when properly applied in suitable cases, especially if one does not wish to destroy cervical function. Where, on the other hand, one wishes to destroy function, the matter is quite another affair. Under these circumstances, cautery must be deep and thorough, or, if the cautery knife be used, it must go deep enough to destroy all the glandular tissue. Thoroughness is here the keynote.

However, in those more numerous cases where cautery is used to re-establish normal cervical function, the limits of this form of treatment

are very circumscribed. An excellent result can be anticipated only in those cases that are mild, and limited chiefly to the surface epithelium lining the cervical canal: chronic catarrhal endocervicitis. It is most effective in nulliparas, and in early treatment after each delivery. It becomes progressively less effective the more widespread the disease, the deeper it has involved the cervical stroma, and the greater the organic departure of the cervix, as a whole, from its normal size and consistence.

It has been stated, in the subject of pathology, that in the great majority of the milder cases the pathologic changes are more pronounced at the canal surface, and that the glands are more normal the deeper one recedes into the cervical parenchyma. This can be demonstrated in a very large percentage of chronic mild or recent subacute inflammatory implantations. This is just the opposite of

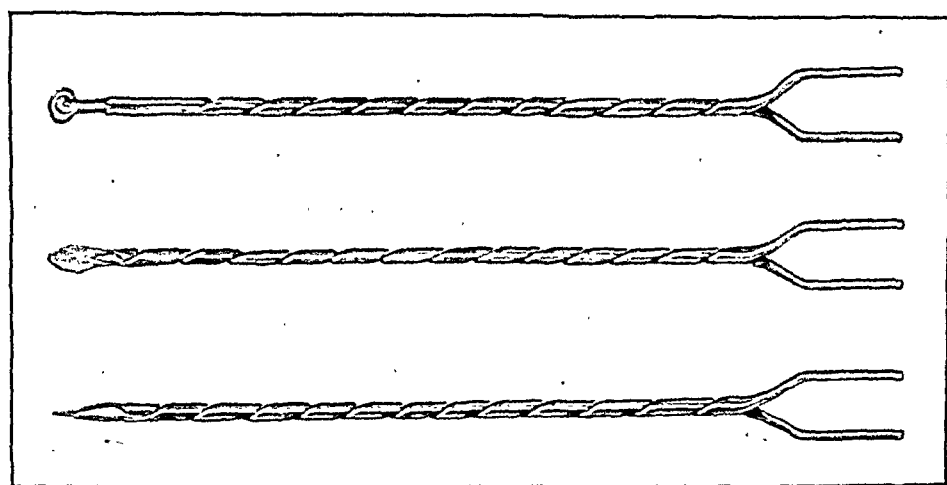


Fig. 9.—Cautery points used by authors in the cure of chronic catarrhal endocervical lesions. The instruments are heated only at the extreme one-half inch. The shank is never more than warm. Natural size.

what happens in the endometrium, where the surface sheds its diseases but allows them to become permanent in the deeper layers. The cervix, therefore, conforms to the general rule of tissues. The uterus is the exception, owing to its special function.

Now, it is just in these mild chronic cervical canal diseases in nulliparas and in recent subacute infections that treatment has proved most effective. In such cases logical treatment destroys the surface layers, and allows the deeper-set normal glands to regenerate a new lining, which they will do, most effectively, if not destroyed. A minimum of scar tissue is caused by such treatment. In nulliparas, one should be careful not to cauterize the external os overvigorously where there is no ectropion. Where, on the other hand, there is ectropion, there is no such risk because the larger the area of ectropion, the more will the external os be patulous and soft. In cauterizing the canal it is not necessary to cleanse the canal of mucus

with caroid or other solvent. In fact, fluid in the canal is a great advantage, for, when it boils, it distributes the heat equally and generally over all the interstices of the canal, so that there is no necessity of bringing the cautery point into contact with the canal epithelium at all. When the canal presents a whitish or parboiled appearance, the treatment has progressed far enough. Treatment so effected will not produce a pocketed and tortuous cervical canal, because the heat is evenly distributed. Frequently, in the next ten days, a thin cast of the canal is shed or the necrotic tissue is disintegrated, leaving a pink healthy mucosa. Care not to constrict the external os is effected by using the cautery type as illustrated below (Fig. 9), where only the wire top is heated. In these cases especially, but preferably in all cases, the cautery should be introduced cold, having previously ascertained the degree of current necessary to effect a dull red heat. The objects of the cauterization are not only to destroy the diseased cervical mucosa, which is the seat of irritative hyperfunction or hyperplasia, but also to destroy the subjacent hyperanemia and hypervascularity, which can be done effectively only by a dull penetrating heat. A white heat will not only just scar the surface, but will destroy the platinum points. With proper care these delicate nasal cautery points will last for years. One minute of careless white heat melts the platinum, and destroys the whole instrument. If ectropion has developed, this should be treated by radical tracings from the os outward to, and beyond, the margin of the ectropion. This again should be done in a dull red heat, by a fine knifelike platinum point. The knife should move slowly over the surface and should penetrate only about $\frac{1}{16}$ of an inch, but slowly enough to coagulate the supernumerary subjacent blood vessels. When larger, discrete vessels emerge from, and course over, the area toward the periphery, these should be destroyed with a finer cautery point, at their point of egress. Similarly nabothian cysts should be punctured and the contents caused to boil with prolonged contact. Sterile paraffin is then applied to the cervix and vagina. Douches are not begun until twenty-four hours after cautery. Their efficacy is questionable, but they are generally used. The pressure should be minimal, and lactic acid, 2 drachms to the quart, is very effective.

Cauterization of the cervix should be done as soon as convenient after cessation of a menstrual period. By choosing this time there will be less bleeding, better healing, and less disturbance of the succeeding menstrual phases. If treatment is instituted after the middle of the intermenstrual period, the subsequent menstruation may be greatly advanced, together with an increase in duration and quantity. In cases where there is much edema of the cervical lips and an unhealthy pale appearance of the area of ectropion from uterine allergy, cardiac disease, or other cause, the efficacy of cautery may be greatly reduced.

Complete restoration of normal function should be effected, together with pearly whiteness of the ectropic area, in about thirty days. Any disease of the appendages, chronic or otherwise, is a contraindication to cautery. Vaginal and vulvar infections should receive appropriate treatment before applying cautery to the cervix.

Cautery of the cervix is contraindicated in gonorrheal disease, except where it is confined to the cervix, a rare condition and a very difficult one to determine. However, I have seen two cases of gonorrheal septicemia, and one of gonorrheal inflammation of the interosseous membrane of the forearm, cured by cautery of the cervix, where there had never been any peritoneal symptoms or palpable disease of the adnexa. Acute and subacute cervical infections may act as a tonsil, constantly infecting the pelvis with successive bouts of peritonitis and involvement of the appendages. Articular disease may not infrequently owe its origin to an infected cervix. There is a certain risk in cauterizing such cases, but it may be undertaken with caution when the metastatic state is grave, and seems to warrant it, and where the cause and effect have been established beyond doubt. Pelvic abscess after cautery, where an unrecognized appendage disease or a virulent infection is present in the vagina, is not common, but always a possibility. The writer once saw a virulent streptococcic septicemia with a rashlike scarlet fever follow upon a mild cauterization.

2. *Chronic Cervicitis*.—We wish to emphasize not only the inadequacy, but also the harmful results, that may follow deep cautery of the cervical canal with a large cautery or cautery knife, extending from $\frac{1}{4}$ to $\frac{1}{3}$ inch in depth, in the hope of reducing a large hard cystic cervix. In the first place, pathology shows the futility of this procedure, and in the second place, it so cicatrizes the cervix that dilatation at subsequent labors may be greatly inhibited or impossible. Cautery of this heroic type tends to produce cervical cicatricial transverse bands with irregular pockets of secretion, tending to aggravate the progress of the original disease. Cicatricial disease of the internal os, where the mucosa is normally very thin, may lead to hematometra and pyometra. There is no cure for such a large fibrous cervix. Its bulk will greatly reduce after menopause, natural or artificial. Practically all types of cervical inflammatory disease rapidly improve after the menopause, with the cessation of the congestion and flow of menstruation.

3. *Surgical Treatment*.—Surgical treatment for the cure of inflammatory disease is an ostrichlike subterfuge. It removes the disease from the scanning eye, but it bottles it up in the canal. It is almost impossible to remove all the diseased mucosa by the deepest coning out during amputation. Drainage is frequently blocked and healing is frequently only by secondary intention. Amputation of the cervix,

for the cure of endocervical disease, is as dead as the dodo in the larger clinics, but is still all too frequent in the smaller centers and hospitals.

But the worst features are the two complications which so frequently follow upon the cervical operations in the presence of endocervicitis. These are (1) late septic hemorrhage and (2) lack of primary union. How frequently one sees women enter the hospital in comparatively good health for a very "simple" operation upon the cervix! On the eighth to the twelfth day, and sometimes later, septic, uncontrollable hemorrhage follows which resists packing and secondary suturing, and yields only to two or more transfusions. Before its arrest the patient is reduced to a very critical state and anxiety is written plainly on the surgeon. And following upon this or without its antecedent, septic hemorrhage, the whole wound separates and heals by granulation, frequently complicated by a thrombophlebitis. For years I have lectured against cervical amputations and cervical repairs in the presence of chronic mucosal disease. If a repair is deemed necessary, owing to tears (undue importance is attached to these) and there is an associated endocervicitis, this latter ought to be cured first by appropriate methods, and, if cure by cautery is impossible, owing to some cause described in the foregoing paragraphs, then repair should be superseded by something less dangerous and more efficacious.

THE INFLUENCE OF A RESIDUAL INFLAMMATORY CERVICAL DISEASE UPON THE RESULTS OF OTHER PELVIC OPERATIONS

The residual cervix in these cases may act in the same manner as would a subacute or chronic gonorrheal case, only with a stronger tendency to produce postoperative septic hemorrhage and thrombophlebitic and lymphatic invasions. We are just beginning to displace the teaching that gonorrhea is a disease *sui generis*. It has much in common with the more common and usually more penetrating lesions of the streptococcus, especially when the latter has reduced its virulence to the level of the average gonococcal strain.

To show the trend of thought in the past few years, one has but to call to mind the general adverse reaction to leaving a uterus or cervix when dealing with gonorrheal disease of the genital organs. True, operations are infrequent in such conditions. But even today such operations have to be undertaken occasionally, for pain and economic reasons. Experience has taught us that a clean sweep is to be advocated, that is, the removal of all columnar surfaces. Why? Because the residual mucosa may be a constant infected tonsil to the pelvic system. We know today, that many low-grade ascending infections, indistinguishable from gonorrheal disease, are of streptococcic origin, whether they are postpartum or not. Thrombophlebitis is a much more

common complication of pelvic operations when the cervix remains than when it has been wholly removed, because, in the vast majority of instances, thrombophlebitis is a disease of a subacute nature arising out of a chronic or subacute mucosal disease. A little study of results will confirm this. This angle of the problem is fully dealt with in the authors' recent work *Total Versus Subtotal Hysterectomy*.^{*} Chronic inflammatory disease of the cervix usually improves after removal of both ovaries, but in conservative operations upon these appendages, followed by a subtotal hysterectomy, the diseased cervix frequently postoperatively develops a vitiated function, to the great disturbance and annoyance of the patient. In the past three months I have had to remove the cervix in three cases after supravaginal hysterectomy, where an anterior or sequent disease of the cervix set up unpleasant intolerable symptoms. These are partly due to the nutritional changes initiated chiefly by subtotal hysterectomies. Destruction of the cervix at the first operation, or its removal by a more radical procedure, would have obviated the sequelae. It is most removed from our wishes to advocate difficult operations with which the operator is not familiar or in which there resides a large element of conservative fear. But other less dangerous means should be adopted to eliminate the cervical postoperative hazard. What procedure should be advocated? Always the one that is best suited to the combined welfare of both patient and surgeon. This must always remain an individual personal question. But let us not close our eyes and ignore the hazard. It must be met, squarely and fairly in the interests of both patient and doctor. The truth is summed up by the confidential statement of a surgeon to me: "It is *very* comforting to both patient and surgeon when the cervix has been rationally dealt with and *most* comforting when that menace has been successfully removed."

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EVIPAL SOLUBLE ANESTHESIA IN GYNECOLOGY*

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NUMEROUS operations and diagnostic procedures frequently used by the gynecologist in everyday practice require complete anesthesia for brief periods of time. General inhalation anesthetics, with their unpleasant sequelae, require costly apparatus, are difficult to administer, and necessitate the services of an expert anesthetist. For the past year, evipal soluble has been employed in our clinic in all patients requiring an anesthesia of not more than thirty minutes' duration. In a few instances it has been used as preliminary medication or for basal anesthesia in place of morphine and scopolamine or tribromethanol (avertin) premedication. The results have been most gratifying and for this reason I wish to report our experience in one hundred consecutive cases.

HISTORY

Evipal soluble is the soluble sodium salt of a new barbituric acid derivative: N-methyl-cyclo-hexenyl-methyl barbituric acid, first prepared by Weese¹ in 1932. It is widely employed by surgeons and anesthetists in Europe where it is known as evipan sodium. It is not a volatile anesthetic, but because of its rapid destruction in the body, the duration of action is short. Detoxication of evipal soluble is effected by its decomposition within the liver. Thus, in the rabbit, one-half the maximal narcotic dose is decomposed in thirteen minutes. Only traces of the injected substance are eliminated in the urine. In animal experiments, the animals fall asleep within a few seconds after intravenous injection of the drug. In addition to this remarkably rapid onset of narcosis, the duration of the effect is extraordinarily short because of the speedy decomposition. Birds awaken in thirty minutes, and mice in fifty minutes. By-effects on the circulation are absent or inconsiderable. The low toxicity is demonstrated by the excellent tolerance to very large doses in cats. Thus, from 20 to 25 mg. per kilogram body weight induces narcosis of only a few minutes' duration, but the same animals survive 100 mg. or even 110 mg. per kilogram doses of evipal soluble. This unusually low toxicity establishes evipal soluble as a true narcotic. From these data it is evident that the therapeutic index is greater than four. Storm,² in a series of 300 anesthetics in 100 monkeys, noticed no change in blood pressure or only a slight temporary fall. In rabbits the reduction of blood pressure is only 15 to 20 mm. while the pulse remains full and regular. When death of the animal was caused experimentally by deliberate overdosage, respiratory failure first occurred and was followed later by cessation of cardiac action. This order of attack on the medullary centers by an anesthetic is the desirable one, since, as is well known, depressed respiration is easily stimulated to renewed activity. The metabolism, body temperature, alkali reserve and blood sugar level are not affected to any noticeable extent. Stimpfl,³ in reviewing 11 cases in which death occurred during evipal soluble narcosis, concluded that the principal factor was overdosage, especially in the presence of sepsis and severe general organic disease. Reschke,⁴ in describing 2 deaths, concluded that the anesthetic is dangerous when used in acute inflammatory conditions

*Read at a meeting of the Chicago Gynecological Society, May 8, 1936.

or even bilateral Schuchardt incision is made which facilitates the approach tremendously. The principle of thus widening the vulva was already emphasized by Jobert de Lamballe; but the deep vaginoperineal incision according to the technic of Schuchardt is as a rule far preferable, offering an additional advantage in the cases of adherent fistulas, as we shall see below.

2. The base of the bladder can be adequately exposed only if it is sufficiently movable. As a result of the original causative traumatic factor (forceps, etc.), we find not only tears of the bladder wall but also injuries extending deep into the parametrial and paravaginal tissue, causing dense scar formation so that the entire base of the bladder can be adherent inferiorly and laterally. Therefore it is absolutely necessary, and this was known to the earliest operators, to liberate the scars immobilizing the base of the bladder, and thus restore its mobility. Stretching of the scars by means of Bozeman's hard rubber plugs is only of historic interest. It is so much simpler, surer, and quicker to separate them bluntly with the finger or with a cutting instrument. If necessary this can be done through a suprapubic incision (Bardenheuer).

Still better and simpler is the procedure of Schauta who recommended a vertical incision external to the labium majus through which he proceeded to free adhesions by blunt dissection paravaginally up to the os pubis, or if they were fixed to the periosteum of the os pubis, he freed them with a raspator. If the adherent scars are less extensive and in the vicinity of the fistula rather than in the paravaginal tissue, such an accessory incision will not be necessary, and they may be separated in the course of the exposure of the base of the bladder. Formerly I used the paralabial incision of Schauta considerably, with good results. Latterly, as a result of my experiences with vaginal operations for carcinoma, I have arrived at what I consider a simpler and better method, which I have described in my book on *Gynecological Operations*, page 398. On the scarred side or even both sides, I make a Schuchardt incision and then dissect upward with the finger along the mesial wall of the levator ani, which permits an easy separation of the entire scarred area from the levator ani and from the symphysis mesially. If the scarry strands are too dense, a raspator or a scissors can be used. Excessive bleeding is exceptional; if it occurs, temporary packing with Stryphon gauze is usually sufficient as the bleeding is almost always parenchymatous and there are no large vessels in this vicinity. The entire lateral wall of the bladder is thus rapidly and easily mobilized and facilitates the mobilization of the floor of the bladder, so essential for bladder suture. The Schuchardt incision has thus an invaluable double advantage in severe cases. It makes the fistulous field accessible and the extensive separation of paravaginal

OPERATIVE TECHNIC OF VESICOVAGINAL FISTULAS

JOSEPH HALBAN, M.D., VIENNA

IN THE course of years I have had occasion to perform about eighty operations for vesicovaginal fistula, exclusive of sixty cases operated in the Wieden Hospital to be published shortly by Mestitz. This represents a considerable number, if we take into consideration the decrease in the number of fistulas due to improved obstetrics and the perfection of operative gynecologic technic. A series of one hundred and more fistula operations, such as have been reported by previous authors (Simon, Salzer and even larger series by Emmet, 400 cases, Fritsch, Küstner, Bozeman, each 200), are no longer within the individual experience of any single operator.

My earliest experiences in this field were in the period of my assistantship at Schauta's clinic. The methods then employed were quite different from those of today. The patients were fastened in the knee-chest position to the Bozeman's fistula table. We used bronze wire suture material inserted and tied with a special instrument. The technic has been considerably simplified. We now operate in the ordinary lithotomy position and use fine catgut. To a certain extent each operator must develop individually and each operation enriches his experience. Today, I approach a fistula operation with great optimism and with the expectation of obtaining a primary cure in the overwhelming majority of cases, providing certain experiences are evaluated and certain definite principles are adhered to.

It is a great pleasure and satisfaction to a surgeon to cure a fistula, especially at the first attempt. Failure means torture both for the patient and for the operator. One can appreciate what a blessing the present-day methods have brought about in view of such martyrdom as occurred in the beginning of fistula operations (Defenbach operated 18 times; Wutzer 30 times). The good results are due to the simplification of the technic and adherence to three basic principles:

1. Extensive exposure of the fistulous area.
2. Mobilization of the base of the bladder.
3. Correct suture.

1. The exposure of the field of the fistula is accomplished by the correct application of posterior and lateral retractors. If the vagina is narrow or the perineum is high and rigid, or if the fistula lies deep in the vaginal funnel as so frequently occurs in those fistulas that result from gynecologic operations, such as hysterectomy, the following procedure is absolutely indicated. An initial episiotomy or a unilateral

On the other hand, it is not necessary to be concerned about the edges of the fistulas and to try to freshen them. The Fũth method is applicable only for the simplest cases. If the fistulous opening is very large or considerably adherent, the construction of a vaginal cuff does not come into consideration. In these cases we must attempt the most extensive exposure of the floor of the bladder.

3. I believe that there is only one correct way to place the bladder sutures, with the best chance for primary union. That is, to ignore the fistula itself entirely in the placing of the sutures and to sew the anterior and posterior portions of the floor of the bladder right over the fistula. These two portions with their attached vesicovaginal fascia are united by fine catgut sutures in areas uninjured by scars or dissection, usually about 1 cm. from the margin of the fistula. One may bury this with a second row, useful but not necessary. The vaginal mucosa may, if desired, be sutured over this. This is quite immaterial as far as the result is concerned. Occasionally it may be easier to place the sutures sagittally rather than transversely. The tension is, however, usually less in the latter and it is thus preferable. The essential point is to sew healthy bladder wall to healthy bladder wall, taking about half the thickness in the suture and not too close to the fistula. I think this is the basis of the good results obtained with Fũth's operation. The preservation of a vaginal cuff itself plays no rôle but it necessitates sewing the bladder farther out, and this works out well.

Ever since I have convinced myself, as a result of personal experiences and occasional failures, that the principles in the treatment of fistula operations that I have mentioned above are basic, I have had excellent results and have undertaken the operation of even very difficult and unfavorable cases with the greatest optimism. The principles are not new and are recognized by most authors. They can, however, be followed more easily by observing technical details that I have pointed out above. One can thus get primary results better than our previous ones.

Fũth reported 68.2 per cent cures (Kleefisch), Franz over 78 per cent, Schulte over 71 per cent. By following the foregoing rules these results can doubtless be surpassed.

Undoubtedly, exceptional cases occur requiring exceptional methods, as for instance, flap plastics, or the utilization of the uterine fundus, or the cervix for covering, etc. The more one adheres to the principles described, the less frequently will unusual procedures be necessary; even severe and unfavorable cases can be cured by simple suture of the bladder. I have not included in these observations those vesicovaginal fistulas with defects of the urethra or of the bladder sphincter. Such cases require quite special measures for cure, not within the scope of this communication.

scars laterally possible, thus facilitating the lateral mobilization of the bladder. If the vagina is particularly ample and the fistula easily exposed, the Schuchardt incision may be avoidable. It is then sufficient to make an incision in the lateral vaginal wall where the levator ani approaches the vagina, and from this point to proceed along the inner surface of the levator to the scars and then separate them. For difficult cases I can only repeat my most earnest recommendation of the Schuchardt incision and the separation of the lateral wall of the bladder from the levator ani.

Mobilization of the base of the bladder itself is occasionally difficult, particularly in those fistulas resulting from hysterectomy. In these cases the fistulas are high up, usually just underneath the scar which closes off the vagina cranially, that is, in the vicinity of the scarry funnel. Such fistulas are adherent to this scar, and it is obvious that they can be sufficiently exposed only by a free dissection of the portion of the floor of the bladder behind them. In this not uncommon variety of fistulas, the scarred vault must be split transversely, separating the anterior from the posterior vaginal wall. Great care must of course be exercised to injure neither the bladder nor the rectum. If the separation is successful, a finger is carefully inserted into the sac-of-Douglas and separates the posterior surface of the bladder from the anterior surface of the rectum. It does not matter if the peritoneum is opened; there is almost never an infection. One can then draw down that portion of the bladder base which lies behind the fistula, in effect what Jobert de Lamballe called "glissement" or "locomotion" of the bladder, exposing it for the correct placing of the sutures. It is obvious that the portion of the bladder base anterior to the fistula must be exposed as well, a much easier task. Small movable fistulas in the middle of the vagina can be healed by the old method of freshening of the margins. I have practically abandoned this procedure, and I expose the fistulas extensively according to the principle of flap-splitting (dedoublement of the French). This is in most cases easily possible if we stick to the principle which I have laid down for the dissection of the vesicovaginal fascia, to wit: that the fascia is permitted to remain on the bladder and separated with the latter from the vagina. One thus remains in the correct anatomic plane, mobilizing the bladder safely and easily. If the fistula is high in the vaginal vault, the mobilization of that part of the base of the bladder which lies behind the fistula is accomplished as I have described above.

It remains a basic principle to expose and mobilize *both* the anterior and posterior portions of the base of the bladder.

It is immaterial whether one utilizes a cuff of vaginal mucosa or not (Füth method). Those authors who believe that the turned-in vaginal cuff contributes to the closure of the bladder are certainly in error.

CASE 2.—M. S. No. 6270. A child of six years with typical infantile myxedema which had been recognized for some time. The child was being given thyroid extract constantly with the expected therapeutic result. The paternal grandmother had died of carcinoma of the thyroid.

This case seems to show that a peculiarity, one might say a biologic inferiority, of thyroid is transmitted in this family, in one case leading to early infantile deficiency and in another, to malignant disease.²

CASE 3.—No. 5893. This history deals with two brothers of whom one had acromegaly with enlargement of the sella turcica and the other a malignant tumor of the pituitary which had resulted in bitemporal hemianopsia, optic atrophy and obesity and for which he had been operated upon. The daughter of the acromegalic was excessively obese. The nineteen-year-old son of the other was a eunuchoid, extremely tall and fat, with the characteristic hair distribution.

Again we are confronted with the diverse phenotypic end-results of a pathologic hereditary predisposition, influencing the hypophysis in the direction of various diseases. This is another example of the biologic inferiority of the organ in question.

CASE 4.—M. C. Hospital admission No. 7395. A woman of thirty-five years with severe diabetes mellitus. The mother died at fifty-six years of age of Addison's disease, and the maternal grandmother had had diabetes.

CASE 5.—E. von G. Hospital admission No. 5884. A woman of thirty-six years with all the symptoms of Addison's disease, probably not of tuberculous origin. The father had diabetes and years ago had had an operation for tumor of the testicle.

The above observations point toward the fact that illnesses of various endocrine glands may alternate in one family in a remarkable way. Only sufficient analogous material would permit our drawing definitive conclusions. Nevertheless, such observations remind us to pay more attention to this type of material in the future.

CASE 6.—T. K. Hospital admission No. 7157. A girl of twenty was admitted with very extensive hypertrichosis of the face, the breast, the abdomen, back and thighs. Considerable obesity and struma were present. There were no other criteria for the diagnosis of a tumor of the adrenal. Menstruation was perfectly normal. Two maternal aunts had been operated upon for Basedow's disease. Two cousins of the mother suffered from extreme obesity.

This case is closely allied to Cases 4 and 5 and requires no further discussion.

CASE 7.—V. W. Hospital admission No. 6703. A woman of thirty-one years complained of a severe alopecia. In addition, she had quite a mustache and a hypertrichosis of the legs, also a struma, a hypoplastic uterus and she was sterile. The mother of this patient had had similar alopecia for twenty-five years and had had an operation for struma.

It is obvious that this rare anomaly of hair distribution has nothing to do with the goiter. This anomaly of the definitive peripheral end organ is one of the signs of what I have called "endocrine stigmatization" of a constitutional variant, having a general influence on the entire hormonal regulatory system. Sometimes this strikes the gland of internal secretion itself, sometimes its peripheral sphere of activity.

The hereditary relationships of cryptorchidism are of particular interest in this connection. This dystopia of the testicle, a retarda-

CONTRIBUTION TO THE PROBLEM OF HEREDITY OF ENDOCRINE DISORDERS

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IT HAS not escaped the attention of previous authors that hereditary factors were of great significance in the etiology of diseases of the endocrine glands. There are numerous observations and indications in the literature of this fact. It is not our purpose at this time to stress this phase, and we refer the reader to the comprehensive exposition of this subject by Berta Aschner¹ working in our division. In this report it was definitely established statistically that in families in which Basedow's disease occurred, simple goiters were found more frequently than the normal expectancy and vice versa in families in which simple goiters occurred; hyperthyroidism was more frequent than the average, i.e., that there was a genotypic relationship between the two illnesses.

It is well known of most of the endocrine illnesses, that they can appear frequently in one family, be genotypically determined. Among these are myxedema, Addison's disease, hyperfunction of the adrenal cortex with intersexuality, precocious puberty, acromegaly, pituitary dwarfism, etc. The marked hereditary factor in obesity, diabetes mellitus and in rare cases of diabetes insipidus is also well known. The modern science of heredity no longer considers the investigation of the special type of hereditary transmission the primary problem, but instead, lays its emphasis on the detailed study of the smallest inheritable factors, the so-called genes, together with the establishment of other phenotypic manifestations. Disease, of course, cannot be inherited, only a particular anlage which can result in various phenotypic manifestations as a result of diverse endogenous and exogenous influences. The investigation of these various conditions and the discovery as to what really constitutes this inheritable anlage seems to me at present to be the chief problem in the study of human heredity. Perhaps some examples will illustrate the point:

CASE 1.—Gina. No. 2618. A thirty-six-year-old woman with typical Basedow's disease, diffuse struma with thrill. Pulse 132. Basal metabolism rate plus 75 per cent to plus 99 per cent. Mother also had Basedow's disease. The child of this patient died two days after birth and had a large congenital struma.

This case illustrates beautifully the statement by Aschner cited above in reference to the inheritable disease anlage and its disposition to the formation of goiters with or without hyperfunction.

CASE 10.—G. R. Hospital admission No. 7293. Forty-one-year-old woman with marked constitutional obesity, weighed 124 kg. Both parents and a sister were obese. The son was also extremely fat and had a cryptorchidism.

CASE 11.—W. G. Hospital admission No. 4750. Seven-year-old boy, left-sided cryptorchidism. This boy was not obese. The father has marked obesity, though not tall, weighed 109 kg. Numerous instances of obesity in the father's family. Mother weighed 80 kg.

CASE 12.—R. S. Hospital admission No. 5277. Ten-year-old boy, right-sided cryptorchidism, obesity; fat distribution typical of a eunuchoid of this age. The father, paternal uncle, and six of eight paternal aunts were markedly obese. One of these had a son with a typical pituitary dwarfism, without obesity. A cousin had had an operation for cryptorchidism at the age of ten.

The preceding case histories are only a fraction of the material that we have observed in recent years. Because of the relatively small number, they prove nothing and can lead to no definitive conclusions. The sole purpose of these notes is to focus the attention of authors to the highly interesting relationships between heredity and the endocrine glands and to stimulate them to collect sufficient material, so that at some later time an impeccable statistical evaluation will be possible. However, I feel that one conclusion is justified: that it is impossible to ignore the facts gleaned from the study of heredity or to practice endocrinology without a detailed knowledge of heredity.⁴

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MARIANNENGASSE 15.

tion in development, is occasionally found in a number of members of the same family. In addition, it shows quite unmistakable connections with other genotypically conditioned, that is, constitutional disturbances in such families. It is not a mere coincidence to find various disturbances of sexual differentiation in the members of the families of cases of cryptorchidism. These may be eunuchoids in whom the gonads persist in an infantile state, or retardation of development of the gonads secondary to pituitary influence or anomalies of the psychosexual constitution, for instance, various forms of perversion. It would seem, then, that the gene responsible for the development and ripening of the testicle must, in some way, be integrated in another complex of genes which have different functions to fulfill, nevertheless representing a common biologic unity. On the one hand, we are dealing with those *anlagen* responsible for normal sexual differentiation. On the other hand, there are obvious relationships between cryptorchidism and constitutional obesity. As I have repeatedly remarked in more detail,³ the assumption seems indisputable that the anlage of obesity is to be understood in this sense, that an individual left to his automatic regulation acquires a more or less excessive increase in weight in the form of an excessive fat deposit which fact is inevitably predetermined in the germ-plasm. This genotypic predetermination to obesity shows its end-results on various organs concerned with fat production and the regulation of its deposit. Among these are the fat-storing mesenchymal tissues, a series of glands of internal secretion regulating such storage and certain portions of the vegetative nervous system. The gonads belong to the circle of organs affected by the pathologic disposition to obesity. It is thus, and thus only, that we can understand why retardations of development and other constitutional disturbances of the gonads are not infrequently found associated with constitutional obesity, without the necessity of attributing the obesity directly to the disturbances of the gonads. It is much more likely that it is the expression of an outranking genopathy and belongs to the category of those constitutional variants which we have designated as endocrine stigmatization. The following family histories illustrate this point:

CASE 8.—A. H. Hospital admission No. 5792. Thirteen-year-old boy with abdominal dystopia of the right testicle. Father was a transvestist and sadist, wears lingerie, etc., and a corset. Both the father and grandfather are heavy drinkers.

CASE 9.—E. F. Hospital admission No. 5197. Ten-year-old boy with right cryptorchidism and obesity. Within the next two years, there was spontaneous descent of the testicle. The father of this boy had a very late development and noticed pubic hair only at the age of eighteen. His genitals were always considered ridiculously small. The mother was a short, fat woman, weighing 90 kg. The brother was fat and weighed 5 kg. at birth.

4. Greater danger to vital organs.
5. Greater difficulty if the pelvic organs are fixed deeply in the pelvic cavity or if the patients are too obese.

An analysis of the above tabulations leads us to the conclusion that the cause of these disadvantages lies in the difficulty of removing the cervix by the abdominal route from its parametrial and vaginal attachments, and also in the difficulty of obtaining proper hemostasis in this region. Even in cases where the cervix is fixed intraabdominally as a result of inflammatory processes, or where adherent retroperitoneal cervical fibroids or adnexal masses are present, the cervix can be more readily

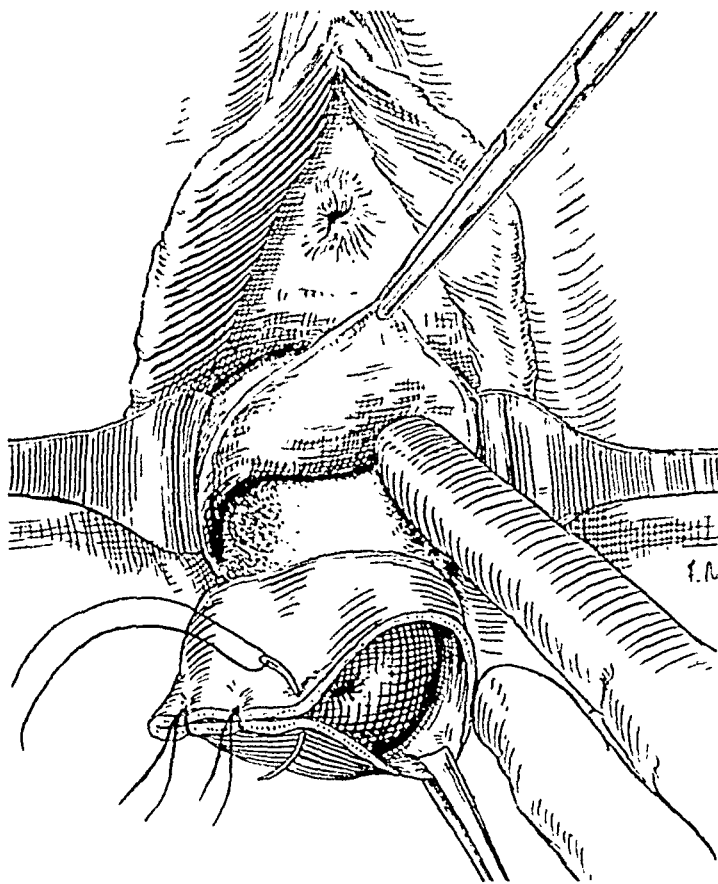


Fig. 1.—Illustrating circular incision about the cervix with mucosal cuff turned down over cervix, and liberation of the bladder from the cervix.

liberated and the parametria and uterine vessels more easily tied by the vaginal than by the abdominal route. It occurred to me that a combined operation would help solve the problem, obviating the difficulties outlined by Goodall and simplifying the procedure so that gynecologists could approach the operation of complete hysterectomy with less reluctance.

TECHNIC

The first stage of the operation is similar to that of a vaginal hysterectomy. The preparation preferred is thorough iodining of the vulva, thighs, perineum, and vagina. A circular incision is made circumscrib-

A COMBINED OPERATION FOR COMPLETE HYSTERECTOMY

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THE respective merits of abdominal supravaginal hysterectomy and complete hysterectomy have been the source of considerable discussion for many years. It seems agreed that there is a slightly greater risk to the patient when a complete operation is performed, though Goodall has recently published a very excellent report, with no operative mortality. In addition to the question of greater operative mortality and morbidity, other problems involved in the decision to perform either a complete or a supravaginal hysterectomy are of importance. The possibility of overlooking a beginning cervical carcinoma while slight is still a danger, and the subsequent development of a carcinoma in the retained cervix, especially when it is lacerated or eroded while infrequent, does occur. Furthermore, a cervix, the site of a persistent inflammation, should be removed. The "coning out" of the cervical mucosa alone is not as complete a procedure as the actual removal of the diseased organ. In other words it is of advantage in many cases to do a complete rather than a supravaginal operation.

Richardson has clearly pointed out the indication for both vaginal and abdominal complete hysterectomy. He stressed that in properly selected cases a skillfully executed total hysterectomy by the vaginal route is a decidedly less formidable procedure than is the same operation performed with equal finesse by the abdominal route. He also states that "in the nulliparas, complicated pelvic pathology tremendously increases the technical difficulties." In addition even in women with roomy vaginas, extensive and dense abdominal adhesions render the vaginal route unsuited for hysterectomy. In the presence of large ovarian neoplasms of solid or cystic type, the vaginal method is also inadvisable. Fibroid tumors when larger than a four months' gravidity, while they may be removed by morcellation, offer considerable technical difficulty. The vaginal approach also precludes the proper inspection of the abdominal cavity. From this array of facts one must conclude that while vaginal hysterectomy is a procedure that must be part of the surgical repertory of every gynecologist it is limited in its applicability. However, the disadvantage of the abdominal complete operation impels us to develop a technic that will facilitate the procedure and reduce to a minimum the disadvantages encountered. Goodall has tabulated the disadvantages of abdominal complete hysterectomy as follows:

1. Greater time expended at operation than for supravaginal hysterectomy.
2. Greater skill required.
3. Greater blood loss.

of the upper respiratory tract since a barbiturate given intravenously may cause laryngeal spasm, resulting in severe respiratory obstruction. Weber,⁵ in discussing the use of evipal soluble in obstetrics and gynecology, estimates that the drug has been used about 800,000 times, of which 12,000 administrations have been in France. He claims that only 4 deaths can be fairly attributed to the drug. Without a doubt there have been over a million administrations up to the present.

DOSAGE AND METHOD OF USE

The prescribed dosage calculated for body weight is 6 c.c. of the 10 per cent solution per 100 pounds of body weight. Evipal is supplied in ampules of 0.5 gm. and 1 gm. of the sodium salt, known as evipal soluble. By the addition of 5 c.c. of sterile distilled water to the 0.5 gm. ampule or 10 c.c. to the 1 gm. ampule shortly before use, a 10 per cent solution is made; each cubic centimeter represents 0.1 gm. of the drug. This solution is aspirated into a sterile glass syringe and then slowly injected into one of the veins in the bend of the elbow. The intravenous injection of evipal soluble does not cause any changes in the vessel wall even if the fluid is retained at the area of injection.

In the past few months this method of determining dosage on body weight has been changed to the following procedure in which the dosage is based upon the response of the patient to the anesthetic agent. The patient is asked to count slowly but audibly. The prepared solution (10 per cent) is injected into the vein at the rate of 3 c.c. the first minute. When the count stops, which is usually before 50 is reached, the dosage administered is noted and an equal amount may be given. This will cause surgical anesthesia with complete relaxation. If the operative procedure is lengthy then additional small (1 or 2 c.c.) amounts may be given when the anesthesia begins to wear off. In our cases we have never used over 10 c.c. of the 10 per cent solution in a given case at one time.

As a basal anesthetic, 3 to 4 c.c. are administered to the patient in her room. This produces sufficient relaxation and narcosis so that she may be easily transported to the operating room and not experience the mental torture of this journey or the fear and discomfort associated with the application of an ether or ethylene mask. When a hypodermic of morphine with or without scopolamine is used, a smaller amount of evipal soluble is necessary but greater care is needed in determining the dose. For this reason we do not employ preliminary medication. Evipal soluble as a basal anesthetic decreased to a minimum the amount of ethylene or drop ether. Relaxation was more complete and the patient's postoperative course was made easier because of the improved mental attitude. Sleep comes on quietly and quickly, the patient often yawning as though falling into natural slumber. Twitching of the face muscles and slight generalized movements may occur for a few moments. Muscular relaxation

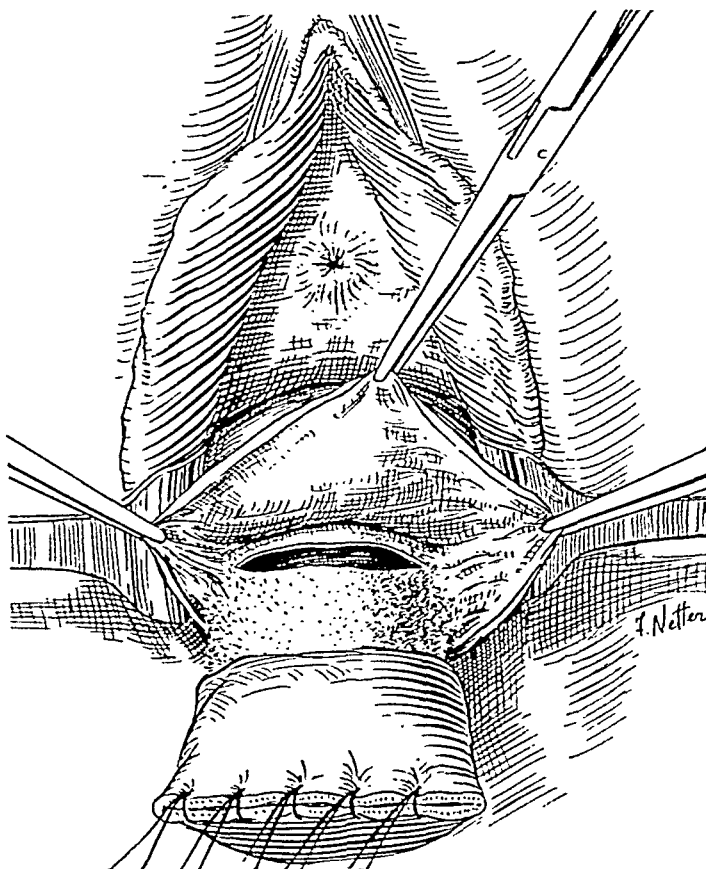


Fig. 2.—Vaginal cuff completely closed, bladder freely liberated. Anterior culdesac incised.

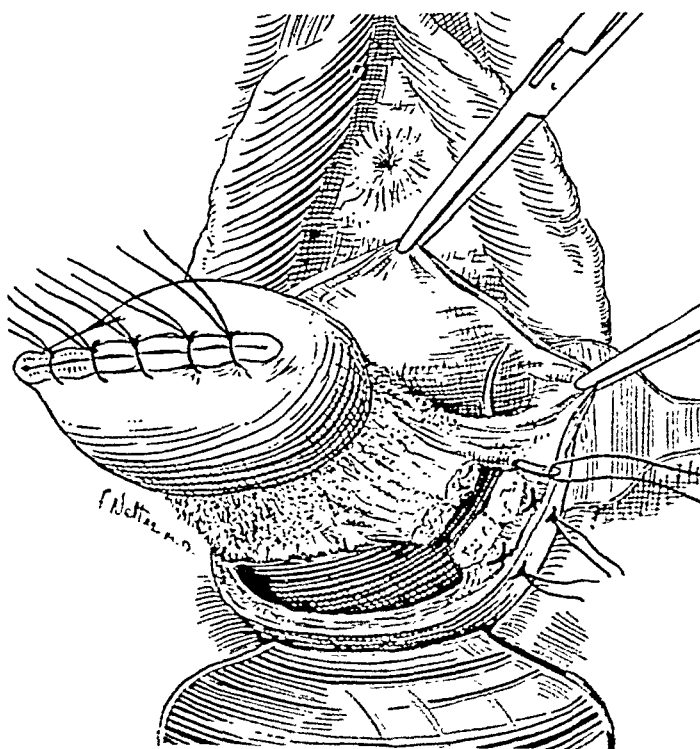


Fig. 3.—Posterior culdesac opened, sacrouterine ligament and parametrial tissue ligated, cut, and anchored to the vaginal wall. Suture placed about uterine vessels.

ing the cervix, leaving a cuff of vaginal mucosa about three-fourths of an inch wide. This is dissected free so that it can be united in front of the cervix with a running stitch thus covering the infected cervix, which must subsequently be delivered through the abdominal cavity. The bladder is pushed upward and the uterovesical peritoneal fold is exposed and opened (Figs. 1 and 2). The posterior culdesac is also widely opened (Fig. 3). Sutures are passed through the posterior portion of the parametrium, one on each side, catching the uterosacral ligament which is cut and freed from the cervix. A second suture is passed through the parametrium above this ligament up to the uterine vessels and the tissue

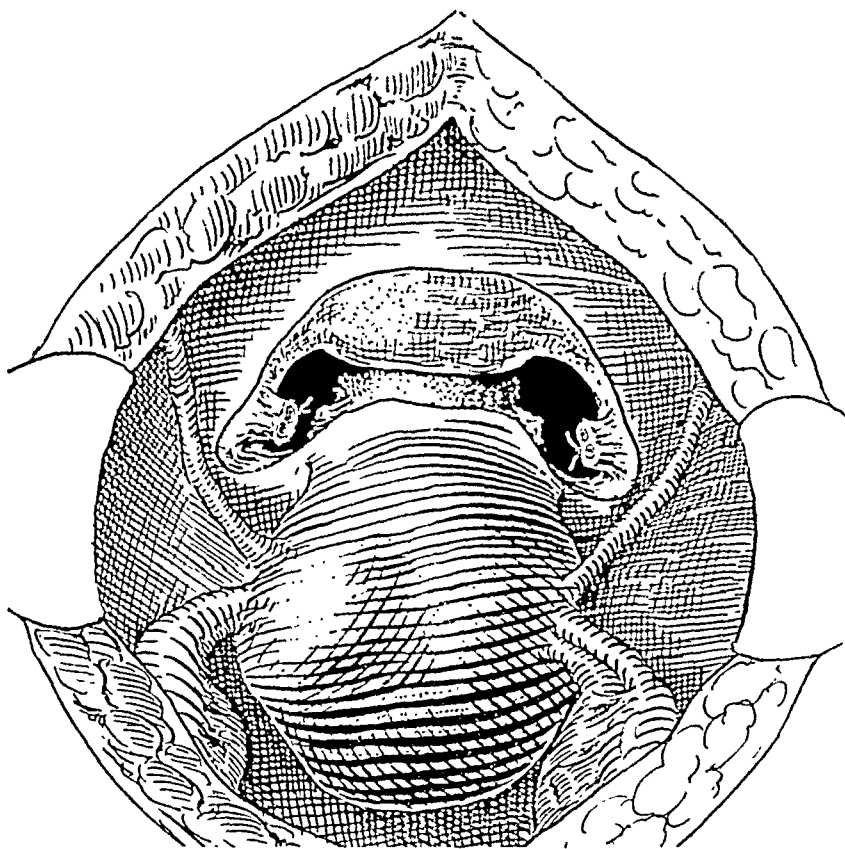


Fig. 4.—Appearance of pelvic floor with the abdomen open after completion of vaginal procedure. Anterior view of uterus showing liberated exposed cervix. The bladder dissected free and the uterine vessels tied.

severed. This may be unnecessary at times if the parametrium is not voluminous. The uterine vessels can now be ligated with either one or two ligatures on each side and cut close to the cervix (Fig. 3). This completes the vaginal procedure except for fixing the parametrial and sacrouterine stumps into the posterior vaginal edge (Fig. 3). The opening in the vaginal mucosa may now be diminished in size by a few interrupted sutures. A large iodoform packing is placed in the vagina up to the everted vaginal mucosal cuff. The patient is now placed in Trendelenburg position and prepared for laparotomy in the routine fashion.

On opening the abdomen the conditions which could not be readily handled if the vaginal operation was continued, such as adhesions, large uterine tumors or ovarian neoplasms, can now be readily taken care of. The infundibulopelvic ligaments are ligated and cut and the round ligaments also. We now find the uterus attached by a few shreds of tissue, usually a small strip of peritoneum on either side and some bundles of connective tissue, i.e., the untied upper portion of the parametrium (Figs. 4 and 5). These are easily cut usually without ligation and the

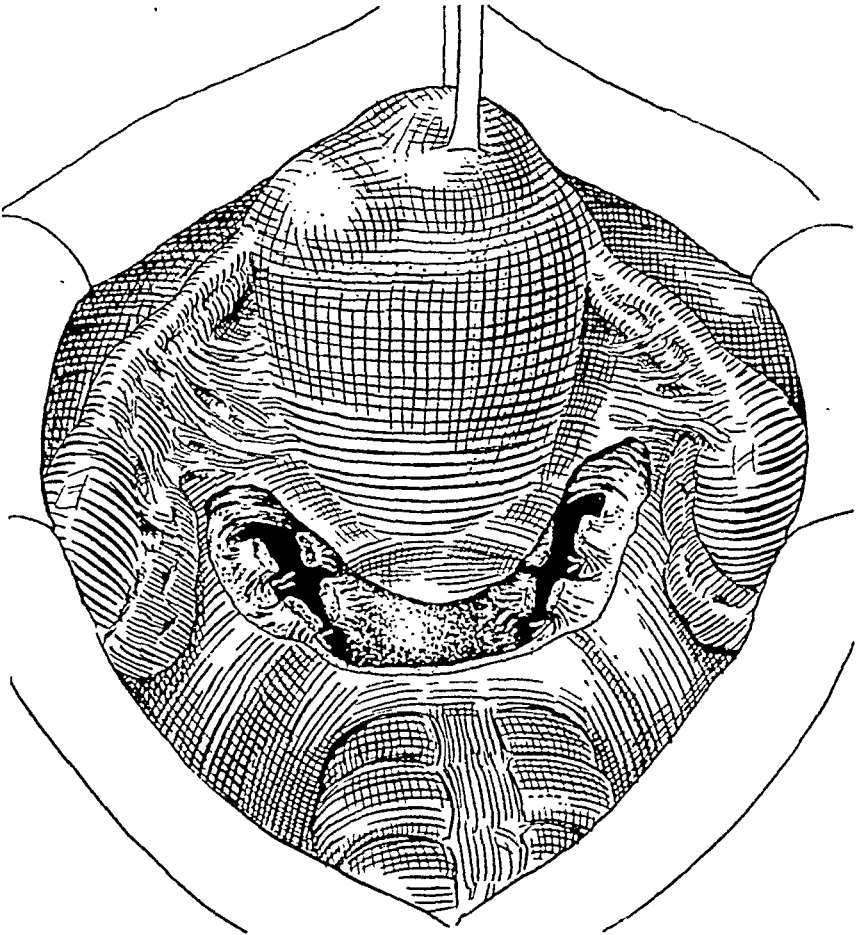


Fig. 5.—Illustrates the condition of the pelvic floor after completion of the vaginal procedure. Uterus drawn forward showing the liberated cervix, the cut and ligated sacrouterine ligament and parametrium.

uterus can be lifted out of the abdomen. The vaginal gauze is removed from below and two narrow strips of iodoform gauze are passed into the vagina on a passer and the abdominal ends of the gauze placed one in each parametrial extraperitoneal space for drainage. If the vaginal opening is still large it can be made smaller by a few sutures. The pelvic peritoneum is closed and the abdominal wall sutured in the usual fashion.

This method makes the access to the uterine vessels simple when an involved inflammatory case or a retroperitoneal or intraligamentous growth prevents easy exposure. The additional time required is negli-

gible. The combined operation which I have had the opportunity of doing only twice took but little more than one hour in both instances. In one case the patient had huge fibroids, one cervical in situation, and in the second case bilateral diseased adnexa adherent to the Douglas peritoneum were present. It is even possible when the posterior vaginal mucosa is incised vaginally to free such growths more readily than from the abdominal side. While the procedure seems to me to offer much, my experience is so limited that I must ask other gynecologists to try it, improve it, and I hope confirm my belief in its advantages.

100 EAST SEVENTY-FOURTH STREET

UTEROTUBAL INSUFFLATION IN THE MACACUS RHESUS

A METHOD OF ASSAYING PHARMACOLOGIC AND HORMONAL EFFECTS ON TUBAL AND UTERINE CONTRACTIONS. A PRELIMINARY REPORT

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PROBLEMS essentially mechanical and physiologic which have arisen during uterotubal insufflation in women appear to be capable of elucidation by studying the results of the application of the same procedure in the monkey. The experimental solution of the physiologic problems depends upon whether contraction waves of the intact uterus and tubes of the monkey can be recorded on the kymograph in a way similar to their clinical demonstration and upon the comparison of these waves with contractions exhibited by the surviving excised genital organs. If this is possible, it should provide a method of assaying in vivo physiologic effects of certain oxytocic, antispasmodic and other pharmacologic substances commonly employed in clinical medicine.

The present study was undertaken to determine whether this method of investigation is feasible and also to note possible changes in rate and amplitude of the tubal and uterine contractions at various stages of the cycle. Incidentally it was felt that certain phenomena observed in the human during uterotubal insufflation might also be checked and possibly explained.

At the outset we were confronted with finding the most practical method of exposing the cervix. Dickinson's observations from a study of thirty adult monkeys showed that the human and simian portio vaginalis bear marked similarities. For cervical inspection alone, the use of Dickinson's modification of the Cushing double-blade nasal speculum sufficed. However, this instrument encroached upon the available space to such an extent as to interfere with the manipulations required for uterotubal insufflation. In order to provide adequate exposure and better to visualize the cervix we resorted to the use of small rectangular, ribbon retractors to draw back the anterior and posterior and also the lateral vaginal walls.

In our experiments the animal anesthetized with nembutal given subcutaneously is placed in the knee-chest position on a triangular block, the cervix is exposed and each lip is grasped by an Allis clamp carry-

ing three or four teeth. The cervix of our parous animals could then be readily pulled downward to the introitus. As was first noted by Sir Arthur Keith and later by Clark and Corner, Dickinson and others, there projects from the anterior or ventral wall of the cervix of the macaque a firm polypoid-like projection, the colliculus. This projection into the cervical canal, as has been emphasized by Dickinson and Engle, offers a definite obstacle to the passage of any instrument and it defeats all attempts at introducing a cannula into the uterine cavity. In order to overcome this difficulty we exposed the colliculus by splitting the cervix bilaterally nearly to the upper border

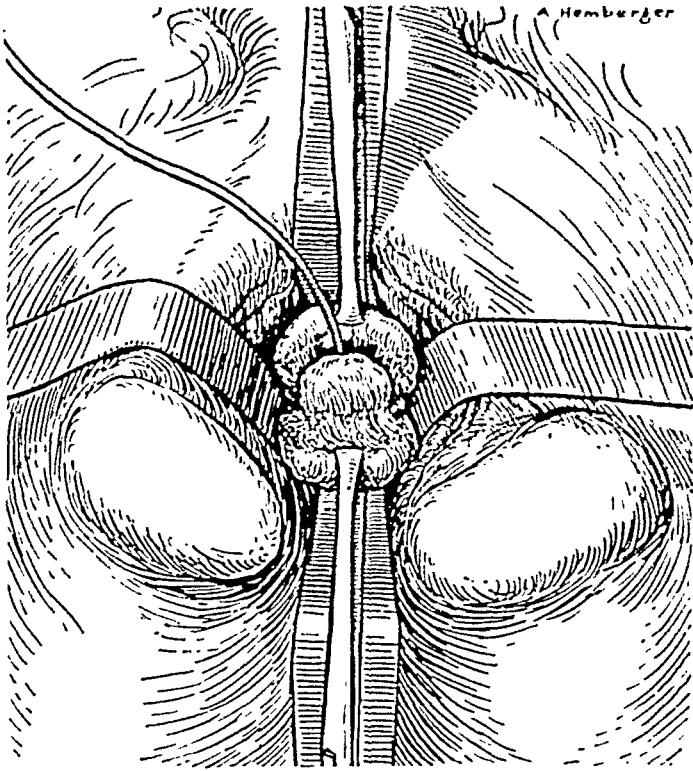


Fig. 1.—Multiparous monkey. Knee-chest position. Cervix drawn downward. Colliculus exposed by retraction of cervical lips following bilateral trachelotomy. Probe indicates course of canal above colliculus.

of the projection. These incisions are associated with surprisingly little bleeding, and so far it has been unnecessary to pass sutures for hemostasis since momentary tamponading has been sufficient to control the relatively slight oozing. Some days after operation, the bilaterally cleft cervix resembles the bilaterally lacerated cervix of the human being and makes possible repeated insufflation without occasioning appreciable bleeding.

In the first monkey operated upon in this fashion a tampon was inserted into the vagina and was retained for several days. This prevented the adhesion of the raw surfaces so that a subsequent introduction of the cannula for insufflation was accomplished with rela-

tive ease. In the next experiments a bilateral trachelotomy immediately exposed the upper border of the colliculus. A fine probe which was then introduced showed that, in the animals employed, the length of the uterus from the external os to the fundus varied from $4\frac{1}{2}$ to $5\frac{1}{2}$ cm. The length of the body was a little greater than that of the cervical canal. A somewhat coarser probe was next passed to dilate the uterine opening sufficiently to permit the insertion of the uterine cannula. The preliminary dilatation we have found to be unnecessary through the procedure of grasping the colliculus with a tenaculum and pulling it downward. This straightens out the canal and exposes the opening which is easily entered by the insufflation cannula. The procedure has been adopted as routine and facilitates the experimental work considerably.

The cannula used is about one-third the width of the instrument commonly employed in the human female, and has ample perforations in the tip to permit the free outflow of gas. The tip of the cannula is introduced within the uterine cavity for a distance of not more than $1\frac{1}{2}$ to 2 cm., the rubber or metallic acorn expansion serving to maintain an air-tight adjustment. The apparatus for insufflation is the same as that employed in clinical gynecology and is gauged for a maximum pressure of 220 mm. Hg.*

An additional obstacle to the experimental project was the resistance encountered at the uterine ends of the tubes. It was found necessary to employ in some instances a pressure level of 200:220 mm. Hg several times, and each time to maintain the high pressure for several minutes, before the uterotubal tone was reduced sufficiently to allow the gas to pass into the tubes and peritoneal cavity. In one instance twenty-two attempts were made within a half hour before success was attained. This time interval may be materially shortened by allowing the pressure to rise up to 300 mm. Hg with a slow rate of insufflation, when the gas may succeed in passing through the tubes, whereupon the pressure drops as rhythmic contractions are recorded on the kymograph. The resistance at the uterotubal junction has been found to be high in all phases of the cycle except possibly near the time of ovulation. This still remains a matter for further study, since our experience is as yet limited to a few monkeys.

When the gas passes through the tubes, rhythmic contractions begin to be recorded upon the revolving drum. They are absent during the initial rise of pressure while the gas is still confined to the uterine cavity and do not appear until the uterine ostiae of the tubes have been passed. While the uterus is increasingly distended, it does not exhibit rhythmic contractions. The latter appear only when the uterus

*The apparatus used in these experiments was made by the Grafix Instrument Company, New York.

is lightly or very moderately distended. The gas thus takes the place of an elastic balloon by which pressure oscillations within the uterine cavity can be recorded.

When tubal contractions are exhibited, the animal is suitable for further experiment with pharmacologic and other substances. When tubal contractions are not demonstrable, owing to almost occlusive resistance at the uterine end of the tubes, the uterine contractions

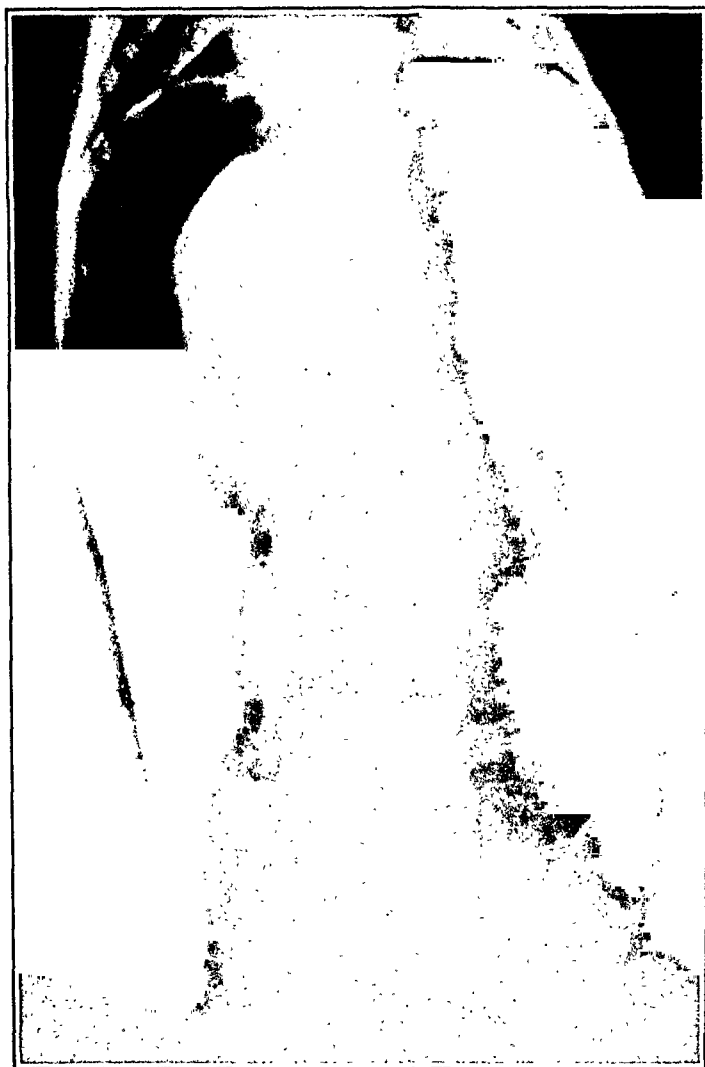


Fig. 2.—Animal 390, showing the distention of the peritoneal cavity by gas introduced by tubal insufflation.

may serve the purpose of the assay. In this preliminary report, we are not prepared to enter into details on this point. However, the effects so far observed from the use of pituitrin and pitocin are prompt and striking.

All the animals which we have employed have tolerated the insufflations well, as much as $2\frac{1}{2}$ to 3 liters of CO_2 gas having been introduced without injury. Following their recovery from the anesthesia, the animals leap about their cages in a typically normal way. In

two animals a laparotomy enabled us to see that the peritoneum was absolutely free of any traumatic or pathologic change, although the abdominal cavity had been distended to drum tightness by 2 to 3 liters of CO₂ gas.

The photographs of Animal 390, taken under the supervision of Dr. Hugh Wilson of the Department of Radiology, show in the first place the distention of the peritoneal cavity which results from the accumulation of gas introduced by way of the tubes, and second, the pneumoperitoneum immediately following the release of most of the contained gas by the insertion of a trocar through the abdominal wall.



Fig. 3.—Animal 390, showing the peritoneal cavity immediately following the release of gas by a trocar inserted through the abdominal wall.

Further experience has indicated the advisability of inserting the trocar for deflation shortly after the gas begins to enter the abdominal cavity. Thus the experiment respecting tubal contractions may be continued without fear of embarrassing respiration. However, if the rate of introduction of gas is sufficiently slow, it may be unnecessary to resort to coincident deflation since the gas is absorbed very rapidly. This rapidity of absorption was demonstrated by repeated x-ray examinations of one of our animals in which the peritoneal cavity, tensely distended at the beginning, showed an almost complete disappearance of the gas at the end of one hour. When uterine

contractions are to serve as the basis for estimating pharmacologic effects, only a minute quantity of CO₂ gas is required—sufficient to fill the uterine cavity under pressures of 60 mm. Hg or less but not enough to produce a pneumoperitoneum.

In the present report, we wish merely to call attention to the method which has been outlined and which within certain limits appears to offer possibilities for experimental purposes along the lines indicated.

We are indebted for assistance to our technicians, Mr. Joseph Negri and Mr. Frank Caruso. The study was subsidized by a grant from the Research Fund of the Yale School of Medicine.

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sets in very early; the jaw drops and, therefore, attention should be directed to keeping it forward or an airway should be inserted. Pain stimuli produced by beginning the operation before the patient is completely asleep necessitate more anesthetic and cause greater difficulty in procuring complete relaxation. Respiratory stimulants and oxygen and 7 per cent CO₂ are always kept at hand but never had to be used in any of our cases.

POSTANESTHETIC COURSE

The duration of anesthesia varies with the dose and physical condition of the patient. The average dose will allow twenty to thirty minutes for operative work. The patient then yawns, stretches, and again sleeps for various periods up to one hour. During this period of recovery, however, she may easily be aroused. If questioned during this time, the answers are often disconnected, resembling those given by one under the influence of alcohol. There is no recollection of what transpired. Mild headache was experienced only occasionally and never persisted. Nausea occurs somewhat more often and is probably due to gagging because of a relaxed tongue or aspirated mucus. Excitement may occur especially if great pain is present, but it can be controlled by suitable doses of morphine. There have been no after-effects in any of our cases.

CLINICAL EFFECTS

The pulse and respiration rates and blood pressure were taken at definite intervals in 20 cases. The average pulse rate increase was 10 while the blood pressure decreased 10 mm. Hg pressure. Respirations after the first minute were slightly slower, averaging from eighteen to twenty a minute. If the patient was overly excited before going to sleep, the pulse and blood pressure were slightly increased as during the excitement stage in inhalation anesthesia. In 2 of our cases the patients were mild diabetics, having preoperative blood sugars above 150 as determined by the Benedict method. No increase in the sugar resulted during anesthesia. Four cases had slight albuminuria before the administration of the evipal soluble, but no increase was noted and there were no microscopic or secretory changes indicating any renal irritation.

The ages of our patients varied from twenty-three to sixty-nine, the majority being over forty. Many with carcinoma were cachectic and anemic. However, in these no ill effects or increased susceptibility to the drug were noted. Severe debility, with heart, liver or kidney disease is, of course, a contraindication to its use.

In the 4 laparotomies performed under evipal soluble no preliminary medication or supplemental anesthetic was used. The operation was begun as soon as the patient was completely relaxed; the prelimi-

output after the twenty-ninth week was maintained, reaching as high as 180,000 M.U. or the equivalent of 18 mg. of crystalline hormones up to the thirty-third week, when a drop to 43,750 M.U. occurred.

It rose again during the thirty-fourth, thirty-fifth, and thirty-sixth weeks to 160,000, and then dropped in the thirty-seventh, thirty-eighth, thirty-ninth, and fortieth week specimens to 39,000, 45,000, 45,000, and 11,200, respectively. Forty-eight hours postpartum, the output averaged 20,000 M.U.

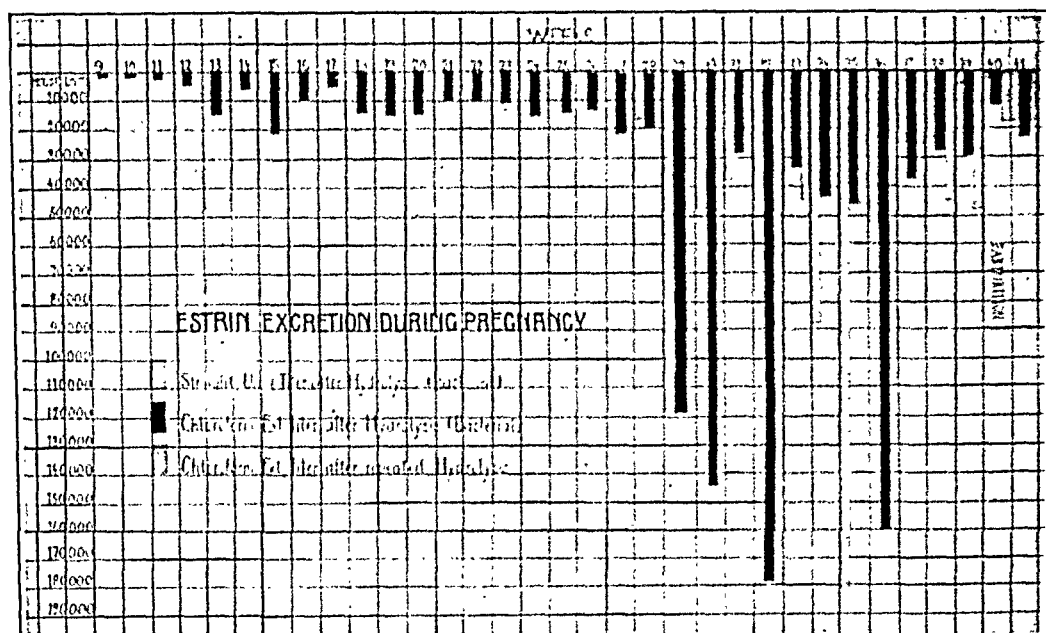


Fig. 1.

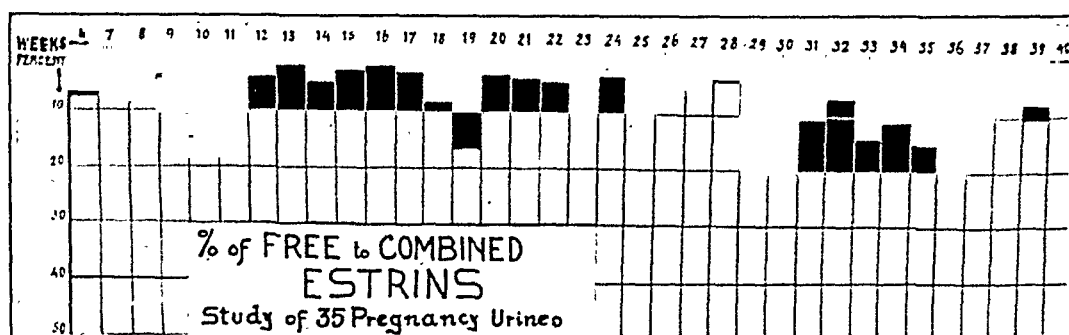


Fig. 2.

The 35 twenty-four-hour specimens assayed at different periods of pregnancy from 35 different women showed that there was a marked variation in the percentage relationship between the free and the combined "estrins" (Chart 2). The free estrins represented from 2 per cent to 22 per cent of the total daily output of active substance. When the total free estrins are compared with the total combined estrins there is an increase in the last eight weeks of pregnancy (Chart 3).

DISCUSSION

Ever since pregnancy urine has been found to contain estrogenic hormones, discrepancies in titer became apparent. Marrian has been

BIOLOGIC ASSAY OF ESTROGENIC FACTORS IN PREGNANCY URINE

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PREGNANCY urine has long been known to contain large quantities of estrogenic substances. Commercially, pure crystalline "estrins" are prepared from such urine. The estrins in pregnancy urine are found in a free and combined state as ketohydroxyestrin (theelin and estrone) and trihydroxyestrin (theelol and estriol). These differ not only in their chemical structure but also in their quantitative biologic activity as well. The free "estrins," according to the conception of Marrian, are those that can be extracted readily from urine with ether. The combined "estrins" are not ether soluble and are extractable with this reagent after hydrolysis of the urine either by acidification and boiling or by means of bacterial action which occurs when urine is allowed to stand at room temperature.

In this study no attempt had been made to separate the estrones from the estriols. It covers the biologic assay of the total estrin output in one case of a normal pregnancy from the ninth to the forty-first week and the relationship of the free to the combined estrins in 35 normal pregnant women at different periods of pregnancy.

METHOD

1. Chloroform extracts of bacterially hydrolyzed pregnancy urine samples were titrated by the Allen and Doisy method in the castrate mouse.
2. Nonextracted pregnancy urine specimens, after bacterial hydrolysis, were titrated as in Method 1.
3. Chloroform extracts of chemically hydrolyzed fresh pregnancy urine was titrated as in Method 1.*
4. Ether extracts of 35 fresh twenty-four-hour pregnancy urine specimens were titrated as in Method 1.
5. Assay of the same urine as used in Method 4 after bacterial hydrolysis.

RESULTS

The continuous study of a normal pregnancy (Chart 1) showed that the total estrogenic output rose slowly from the ninth to the twenty-ninth week from 1,000 M.U. to 20,000 M.U. in the twenty-four-hour specimens examined weekly. Comparing this with the international unit standard, this rise is equivalent to the difference between $\frac{1}{10}$ mg. and 2 mg. of crystalline "estrins." On the twenty-eighth week, antepartum, there was a sudden rise in estrogenic factors to 125,000 M.U. in nonextracted urine and 119,000 M.U. by the chloroform method. The high estrogenic

*Method 3 was carried out for comparison to determine if bacterial hydrolysis is complete.

tracts of urine by means of biologic methods, that it was deemed essential to determine whether biologic assays would show a similar relation.

The biologic assay in this study shows that the total estrins excreted in normal pregnancy is low up to the twenty-ninth week and highest between the twenty-ninth and thirty-sixth weeks. It again drops to a low level in the last four weeks of pregnancy. The free estrin excretion found in this investigation was greatest between the thirty-second and fortieth weeks.

The percentage of free estrins varies from 2 per cent to 22 per cent and shows no definite relationship to the period of pregnancy. Before drawing definite conclusions a large series of cases should be investigated.

CONCLUSIONS

1. There is an increase in the combined estrin excretion as pregnancy advances. This reaches its highest point between the twenty-ninth and thirty-sixth weeks.

2. There is a diminished excretion of combined estrins in the last four weeks of pregnancy.

3. The free estrin excretion is greatest between the thirty-second and fortieth weeks.

4. No constant percentage relationship is noted between the duration of the pregnancy and the excretion of free estrins.

5. Assays of pregnancy urine following bacterial hydrolysis are concordant with those obtained with acid hydrolysis.

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145 WEST 86TH STREET

NOTE

For lack of space it is not possible to include in this issue of the JOURNAL all of the papers contributed to the Robert T. Frank Anniversary Number. Several will appear in the July number and all will be published in a special volume to be issued at a later date by the committee in charge.

able to influence the titer by hydrolysis. This may be accomplished equally well by acidification or bacterial action (allowing urine to stand at room temperature for several days).

Cohen, Marrian and Watson have studied the excretion of the estrogenic factors during pregnancy on samples obtained from 20 different pregnant women. Their method of assay was a chemical one, namely, a modification of Kober's colorimetric assay method. They found that the "estrin" excretion rose rapidly at about the third month, maintained a high level throughout the remainder of the pregnancy, and finally fell to a low level a few days before or at delivery.

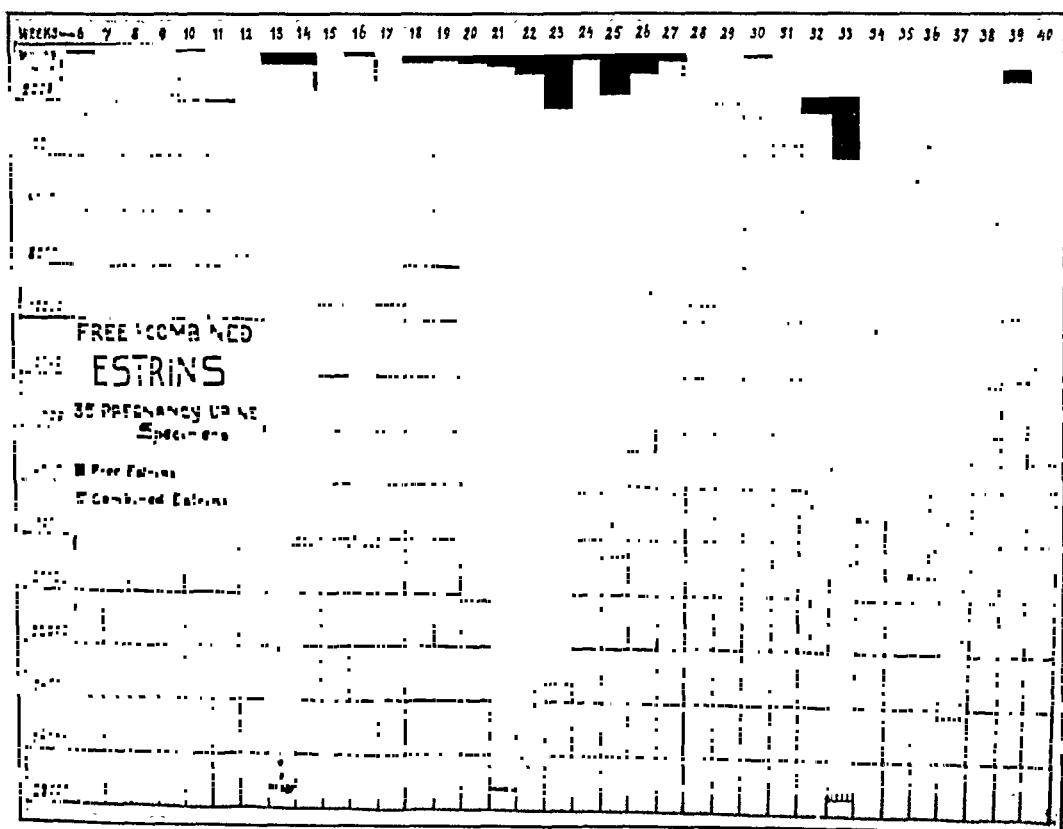


Fig. 3.

From estimations on the quantitative excretion of free and combined estrins and estriols, they concluded that 99 per cent of the total estrogenic factors found in pregnancy urine up to the eighth month were in the combined ether-insoluble form, and, as they interpreted it, physiologically inert. This, they attributed to the ability of the pregnant woman to inactivate estrin. They also suggested that the onset of labor is dependent upon a drop in the combined estrins and a rise in the free forms with consequent contractile effect on the uterine muscle.

The finding of 99 per cent of the estrogenic factors in the combined ether-insoluble form, as reported by these authors, seemed so greatly at variance with our experience in the assay of fresh and chloroform ex-

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nary preparation and draping having been done before beginning the injection. Relaxation was complete, straining entirely absent so that the work could be done easily and swiftly. Postoperative distention was slight and discomfort nil. Nausea occurred once in one case immediately upon awakening.

Several patients receiving radium in divided doses were given the anesthetic three times at intervals of five days. One patient has had the drug seven times over a period of six months. Repeated usage in a patient does not require an increase in the dose or change its effects. However, when given again to the same patient the dosage should depend upon the patient's reactivity and may not necessarily be the same as administered at first since her susceptibility may have changed in the interim. Patients have never protested to its repeated use.

Weber,⁵ Stacey,⁶ Fregyesi⁷ and others have reported the successful use of evipal soluble in obstetrics and gynecology, the latter author having successfully employed evipal soluble with local infiltration anesthesia in 40 abdominal and 16 vaginal operations, which were too prolonged for evipal soluble anesthesia alone. He states that the combination worked ideally in his cases.

CASE REPORTS

Dilatation and curettage and radium	42 cases	Incision of perirectal abscess	1 case
Removal of cyst of breast	4 cases	Biopsy	7 cases
Implantation of radium	10 cases	Proctoscopic examination	5 cases
Cautery of carcinoma of cervix	1 case	Interposition operation	1 case
Appendectomy and uterine suspension	2 cases	Cautery of cervix	3 cases
Appendectomy	2 cases	Removal of papilloma of labia	1 case
Cystoscopic examination	5 cases	Resection of inguinal glands	3 cases
Dilatation and curettage	6 cases	Removal of Bartholin's cyst	1 case
		Basal anesthetic	3 cases
		Subarachnoid alcohol injection	3 cases

CONCLUSIONS

In our hands, evipal soluble has proved a very successful and satisfactory anesthetic for short operative procedures. In the 100 cases reported there have been no harmful effects from its administration. Its effects on respirations, heart action, blood pressure, and blood sugar level have been studied and no marked alterations were noted. In instances where three to five injections have been employed in the same individual, there has been no difference in the patient's response or the effect upon the functions of the body. Evipal soluble is deemed an ideal and safe anesthetic for brief anesthesia.

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OVARIAN PREGNANCY*

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BECAUSE of its comparative rarity, ovarian pregnancy is of great interest. The possibility of its occurrence was not recognized until the seventeenth century, and although cases reported subsequently were apparently authentic, this eventuality was questioned for a long time. Even today, there is considerable controversy and no two authors agree as to what constitutes a true primary ovarian pregnancy.

The case herewith reported is the first seen by me. A search of the records at the New York Post-Graduate Hospital reveals but three additional cases, one reported by Jacobson in 1908 and two unpublished cases. The first was under the care of West in 1924, and the second operated upon by Russell in 1922, and mentioned in this report with his permission. Of 187 patients operated upon for ectopic gestation from 1920 to 1935, but two proved to be ovarian pregnancies. Whether these two were true primary ovarian gestations cannot be determined at the present time, as the laboratory reports filed with the histories, based on present-day standards, are inadequate, and the specimens are not suitable for further study.

In 1917, Mayer and Wynne stated that, from the evidence contained in the literature, it is clear that further case reports of ovarian pregnancy are not needed for the purpose of establishing the occurrence of this condition, but such reports, nevertheless, may help in the determination of the relative frequency of this novel and sinister condition and also throw further light upon its genesis and the finer relations of the implantations.

Ovarian pregnancy has been described as primary or intrafollicular when the sperm cell enters through the aperture produced by the bursting of a follicle and impregnates the ovum which has not escaped, the opening closing and gestation proceeding in the sealed sac; secondary or superficial, when fertilization of the ovum takes place after its liberation from the graafian follicle with subsequent development upon the surface of the ovary.

For the determination of the primary type, the criteria of Spiegelberg, promulgated by him in 1878, were accepted as adequate up to the present century.

*Read before the Section of Obstetrics and Gynecology, New York Academy of Medicine, March 24, 1936.

He demanded that (1) the tube on the affected side be intact and have no organic connection with the gestation sac; (2) the fetal sac must occupy the position of the ovary; (3) it must be connected with the uterus by the ovarian ligament; (4) definite ovarian tissue must be found in the sac wall. In more recent years, Williams supplemented these by claiming that ovarian tissue must be present in several portions of the sac wall. Norris added that the tube on the affected side must not only be intact, but microscopically free from any evidence of gestation. Mapes and others differed from their confreres in that they accepted these concepts with reservations. These exacting requirements had for their object the definite distinction between the true and the doubtful. However, in the final analysis, each individual case must be viewed not only on the basis of the history and operative findings, but also of a careful gross and histopathologic study of serial sections taken from various parts of the specimen.

Because of the foregoing, I feel justified in reporting a case of true ovarian pregnancy.

Case Report.—On Sept. 6, 1935, Mrs. H. S., aged twenty-two years, presented herself complaining of amenorrhea and pain in the midportion of the abdomen. On September 2, she had sudden dizziness, fainting, nausea and vomiting with severe pains in the mid-abdomen above the umbilicus. Her physician, who had treated her for two years for gastric distress, attributed the immediate symptoms to a gastric upset. The menstrual history was negative, her last period occurring on July 28, 1935. She had been married one year, had never been pregnant, used postcoital douches as a contraceptive measure. On physical examination, she showed marked pallor; the abdomen was distended and there was tenderness in both lower quadrants. No masses were palpable. The cervix was slightly softened at the tip, deep in the culdesac, but not tender on manipulation. It showed no discoloration. The uterus was slightly enlarged, somewhat softened, not globular. It was in anterior position, freely movable and not tender. The adnexa could not be palpated. A blood count showed 2,450,000 red blood cells; 7,400 white blood cells and normal differential count; hemoglobin 57 per cent. The patient's appearance suggested bleeding, but she presented no positive evidence of it. As ectopic gestation was suspected, she was advised to enter the hospital. The Friedman modification of the Aschheim-Zondek test was strongly positive. The urine showed no evidence of blood; the stool, Benzidine 4-plus for occult blood, Guaiac test negative. On Sept. 10, 1935, a transfusion of 500 c.c. of whole blood was given which was followed by 3,530,000 red blood cells and hemoglobin 72 per cent. As her symptoms had subsided and repeated examinations revealed no evidence of masses in the pelvis, and her general condition improved, she was discharged from the hospital on Sept. 17, 1935, and instructed to keep under observation. She did not return until Sept. 26, 1935, for examination. On September 24, she noticed severe pain on defecation and this had become progressively worse and more constant. On examination, a very hard mass was found in the culdesac, the origin of which could not be determined. A diagnosis of ruptured ectopic gestation was made and the patient was readmitted to the hospital. On September 27, under gas-oxygen-ether anesthesia, the abdomen was opened through a suprapubic midline incision, starting from the symphysis to $1\frac{1}{2}$ inches below the umbilicus. On opening the peritoneum, no free blood was found. A large mass, the size of an elongated orange, filled the culdesac of Douglas. The uterus was anterior to the mass, normal in contour, position, and color and showed no congestion; both fallopian tubes were in normal position and freely movable. The mass was identified as the right ovary, bluish red in color, hemorrhagic in type, and attached to the uteroovarian ligament, which was somewhat elongated (Fig. 1).

The mass was excised and a prophylactic appendectomy performed. On September 30, three days after operation, a decidual cast was passed through the vagina. She made an uneventful recovery, leaving the hospital at the end of eleven days.

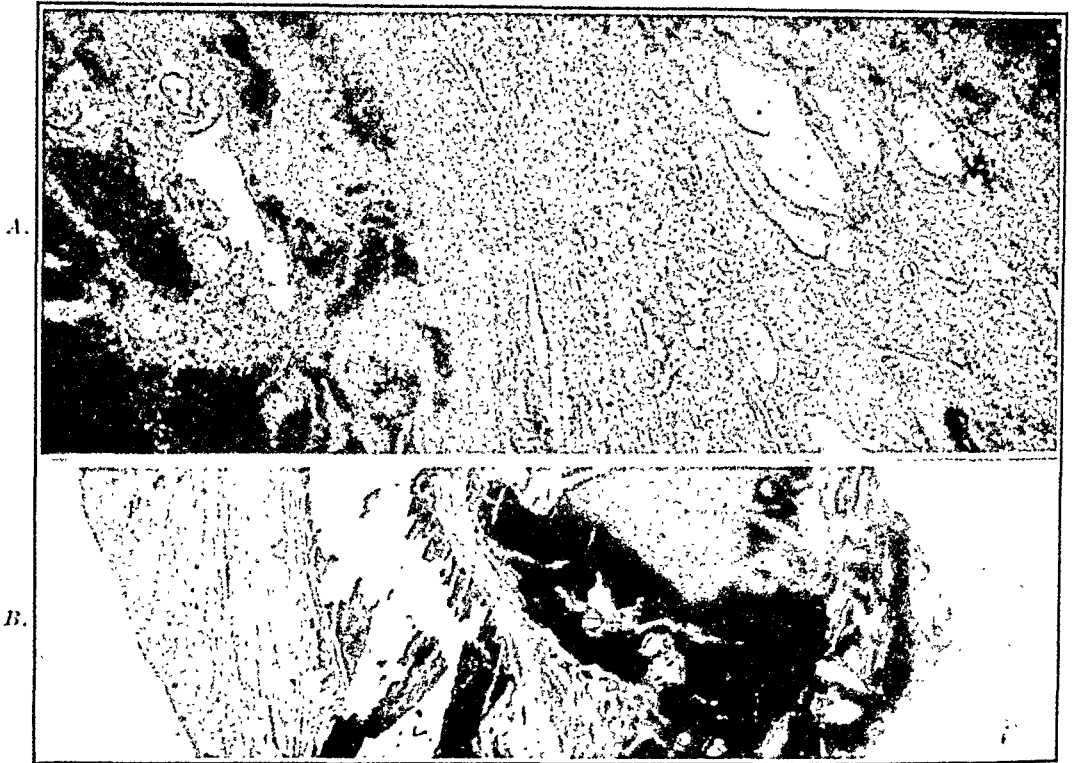


Fig. 3.—A and B. Microscopic Section 1, high power magnification. Shows hemorrhagic cyst to be partly embedded in ovarian substance (right). In the clot one is able to recognize typical fetal villi.



Fig. 4.—Section 2. High power magnification of the thickened portion of the ovarian cortex; shows many layers of large pale lutein cells about a largely centralized central blood clot (left); edematous ovarian cortex internal to the capsule of the corpus luteum with numerous large blood vessels.

The oviduct on the affected side at the time of operation was normal in color and appearance. There was no evidence of congestion or adhesions. The fimbriated end was pinkish in color and it was evident that no pre-existing blood clot had been

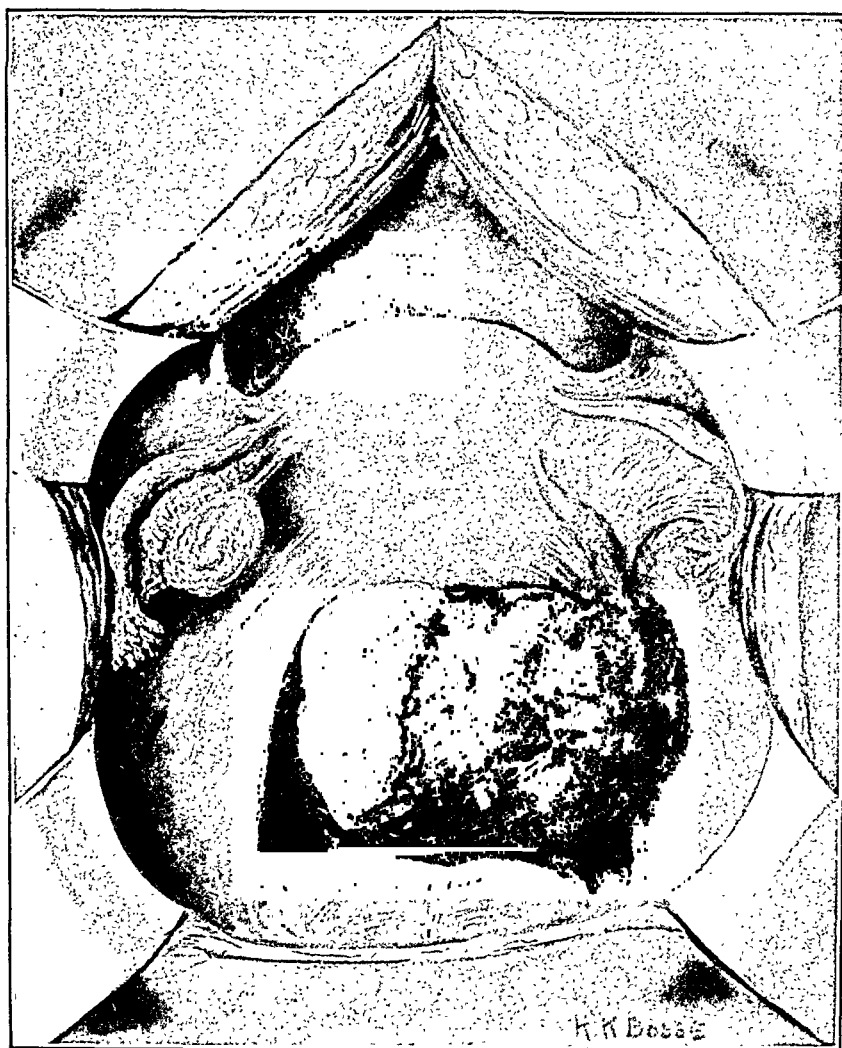


Fig. 1.—Appearance of ovarian pregnancy on opening abdomen.

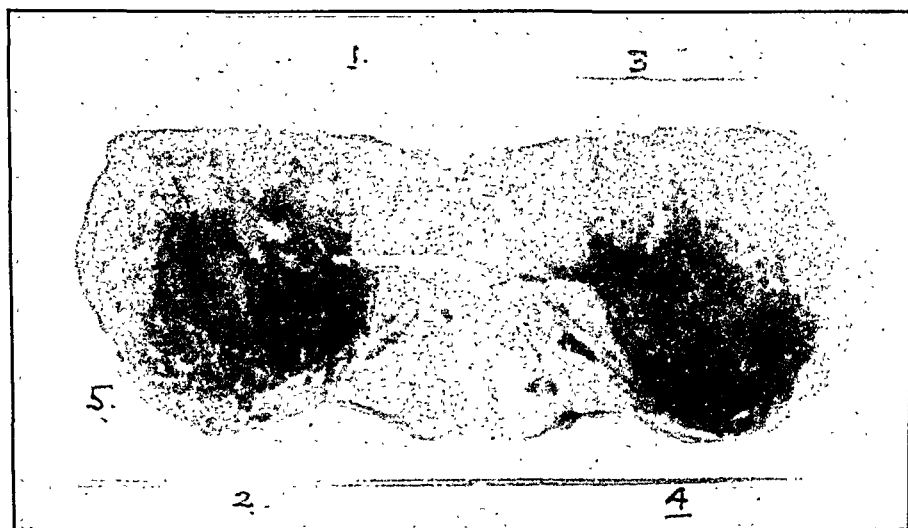


Fig. 2.—Gross specimen. Numbers indicate the five areas from which sections were removed for microscopic study.

was a hemorrhagic cyst attaining a diameter of 58 mm. In the center of this, there was a cavity 10 mm. in diameter with some white opaque material in it and also portions of translucent membrane. One could not recognize an embryo with certainty, but apparently there was a portion of embryo present (Fig. 2).

Microscopic.—Sections as numerically indicated on the gross specimen (Fig. 2) were removed from five different areas.



Fig. 7.—Section 5, low power magnification, directly opposite Section 2, Fig. 4, including the capsule. Shows the partially organized hematoma (left). Throughout the hematoma there are numerous fetal villi, some of which show a basal attachment to chorionic sac (right).

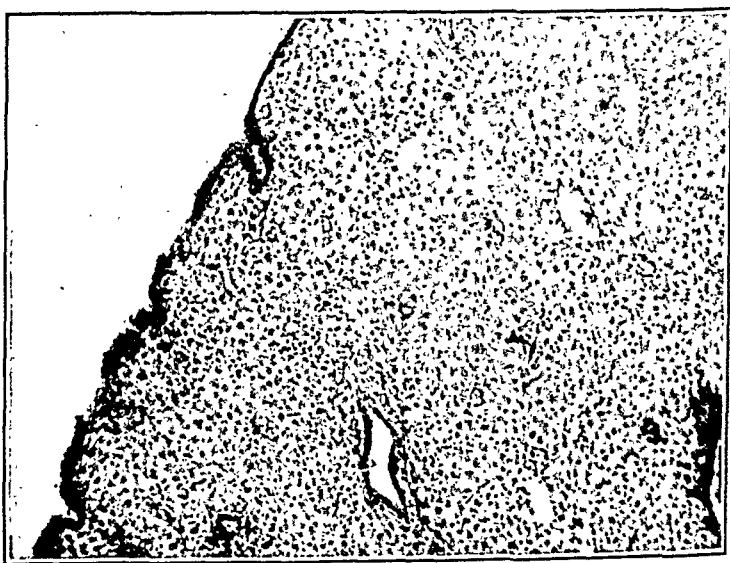


Fig. 8.—Decidual "cast," expelled from vagina three days following operation. Area showing complete replacement of endometrial stroma by decidual cells and sections of glands lined by columnar epithelium which also appears on the surface of the endometrium. There is moderate infiltration by polymorphonuclear neutrophils and to a lesser degree by lymphocytes.

Section 1, high power magnification, showed hemorrhagic cyst to be partly embedded in ovarian substance. In the clot, one was able to recognize fetal villi (Fig. 3, a and b).

Section 2, high power magnification of thickened portion of the ovarian cortex, consisted entirely of many layers of large pale lutein cells about a central blood

present. In the absence of any gross pathology, the tube was not removed. Considering the age of the patient, her social status and the possibility of future impregnation, it was felt that the removal of such a tube just for serial microscopic examination, to determine the existence of a possible pre-existing tuboovarian pregnancy, as advocated by Norris, would have been unfair to the patient.



Fig. 5.—Section 3, low power magnification, from opposite side of the hematoma including the capsule. Resembles Section 1. The capsule (left) is ovarian cortex; abundant blood channels and blood vessels suggest the trophoblastic area seen in the uterus in uterine pregnancy. Just internal to this layer the hematoma (right) contains fetal villi with central myxomatous areas and a covering of syncytial cells.

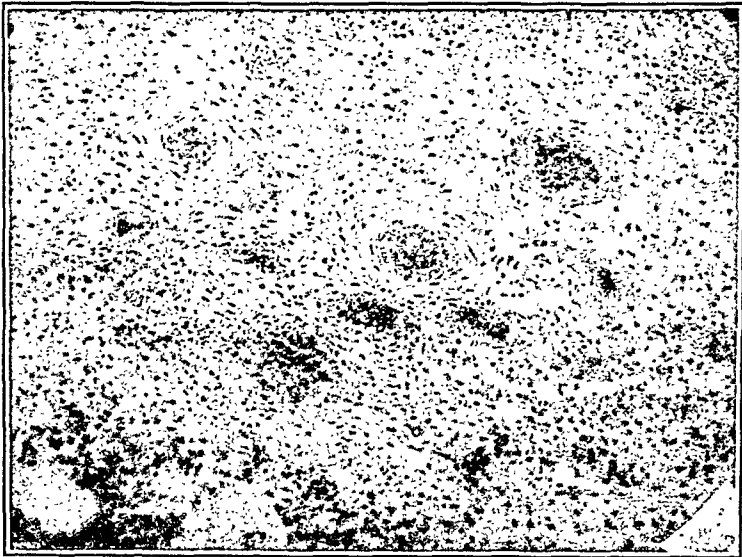


Fig. 6.—Section 4, high power magnification, from margin of hematoma directly opposite Section 3, Fig. 5. Viable portions which are composed almost entirely of large decidua cells.

PATHOLOGIC REPORT

Gross.—Specimen appeared to be an ovary with a large amount of clotted blood adherent to it. The specimen measured over all 50 by 50 by 45 mm. Apparently there was a portion of ovary or possibly entire ovary at one side. On section one recognized a corpus luteum 17 mm. in diameter. At one side of the specimen there

IMPETIGO HERPETIFORMIS OCCURRING DURING PREGNANCY

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AS STATED by Highman,¹⁴ "there are no skin diseases peculiar to pregnancy except certain hyperpigmentations, known as chloas-mata." Any skin disease which occurs in pregnancy and which endangers the life of the patient or of the child, either directly or indirectly, should be of interest to the obstetrician.

In a series of 735 deliveries at Duke Hospital there were two patients with dermatitis herpetiformis, or impetigo herpetiformis, whose pregnancies, deliveries, and postpartum courses were markedly influenced by the disease. According to Irving, no patients with dermatitis herpetiformis, or impetigo herpetiformis, have been admitted to the Boston Lying-In Hospital during the past twenty years. Two case reports by Gellhorn and one by Howard have recently appeared in American literature.

Our first patient was a twenty-five-year-old white, single primipara at term, who was referred to the hospital in labor on Dec. 15, 1933, with a diagnosis of generally contracted pelvis. Uterine contractions had started three days prior to admission, were intermittent for two days, and were hard and regular for the twenty-four hours prior to admission. During the last trimester of her pregnancy she had noted a polymorphous rash which had appeared on her thighs, vulva, and trunk. The lesions were first erythematous macules which became vesicular, with turbid contents, and ruptured. The patient experienced considerable itching. A dermatologist made the diagnosis of dermatitis herpetiformis.

On admission her temperature was 37.6° C., pulse 100, respirations 24, and blood pressure 152/84. She was a well-developed and nourished young white female. There was no peripheral edema. The skin of the abdomen, vulva, and thighs was covered with crusted polymorphous lesions. The most prominent lesions were red macules varying in size from a few millimeters to a centimeter in diameter. The mucous membranes were not involved. The heart and lungs were normal. The fundus rose 30.0 cm. above the symphysis; the fetus was in L.O.A. position. There was no engagement of the head. The fetal heart rate was 132 per minute. Rectal examination showed the cervix to be effaced and three fingers dilated and the vertex not engaged. The membranes had ruptured. Pelvic measurements were: interspinous 21.0; intercrystal 25.0; bitrochanteric 30.0; bituberous 9.0; posterior sagittal 9.0; diagonal conjugate 10.0; and external conjugate 16.0.

Her Wassermann reaction was negative. A catheterized specimen of urine was negative. The hemoglobin was 90 per cent (Sahli), red cell count was 5,000,000, and white cell count was 30,000. A differential count showed 87 per cent polymorphonuclears, 10 per cent lymphocytes and 3 per cent monocytes. There was no eosinophilia.

clot which was largely organized. Internal to the capsule of the corpus luteum there was edematous ovarian cortex with numerous large blood vessels and portion of the wall of the tissue surrounding the central blood clot (Fig. 4).

Section 3, low power magnification, from opposite side of the hematoma including the capsule. Resembled Section 1. The capsule was ovarian cortex with marked increase of fibrous tissue and blood vessels. Abundant blood channels and blood vessels suggested the trophoblastic area seen in the uterus in uterine pregnancy. Just internal to this layer, the hematoma contained fetal villi with central myxomatous areas and a covering of syncytial cells (Fig. 5).

Section 4, high power magnification, from margin of hematoma directly opposite Section 3, Fig. 5. Viable portions which were composed almost entirely of large decidual cells (Fig. 6).

Section 5, low power magnification, directly opposite Section 2, Fig. 4, including the capsule. Showed the partially organized hematoma. Throughout the hematoma there were numerous fetal villi, some of which showed a basal attachment to chorionic sac (Fig. 7).

Decidual "casts," expelled from the vagina three days following operation. Decidual tissue showing purulent inflammation. Areas showed complete replacement of endometrial stroma by decidual cells and sections of glands lined by columnar epithelium which also appeared on the surface of the endometrium. There was moderate infiltration by polymorphonuclear neutrophils and to a lesser degree by lymphocytes (Fig. 8).

Diagnosis.—Ovarian pregnancy.

In the present case a diagnosis other than ectopic pregnancy was not tenable from the clinical findings. Of particular interest is the short duration of pregnancy, and the fact that fourteen days before operation no adnexal enlargement could be detected.

78 EAST 79TH STREET

Larionov, V. F.: *Influence of Placental Preparations on the Egg-Laying of Hens*, Vopr. Endocrinol., Moscow, p. 824, 1936.

The author ran several series of experiments on feeding hens with human and animal placenta in the biologic laboratory of the Scientific Research Institute of poultry breeding. In nine different series of experiments 1,000 hens were used. Results show a definite increase of egg-laying ability. Twenty control hens from January to July 15 laid 848 eggs. The twenty experimental hens in the same period of time before experiment was started, laid 896 eggs. The experiment began July 16 and continued until September. The control hens laid 246 and the experimental hens, for the same period, 348 eggs. Other series showed similar increases under placental feeding. Size and incubation qualities of the eggs of the experimental hens were not altered. To exclude the conclusion that increased egg-laying depends on increased protein intake, control hens were fed the same amount of different proteins, as meat or dried blood in powdered form, but no beneficial effect could be noticed. The author thinks that stimulated ovarian activity is due only to the hormones contained in the placenta, and that continued experiments might show that fresh placenta contains vitamin E.

ALEXANDER GABRIELIANZ.

stated that since the onset of the rash her hair had been "dropping out." There was a firm nodule about a centimeter in diameter apparently attached to the skull posterior to the right mastoid region. There were sparsely scattered crusted lesions 0.5 to 1.0 cm. in diameter on her scalp. On either side of her nose and in the nasolabial folds were small white scars, 2.0 to 5.0 mm. in diameter. The chest and both shins were thickly covered with vesicles, bullae, and crusts. The back, buttocks, thighs, lower abdomen, vulva and arms were covered with brown and red macules, and a few vesicles arranged in somewhat symmetrical patches with scalloped, circinate borders. The posterior auricular, cervical, axillary and inguinal nodes were all enlarged and palpable. The thyroid was not enlarged. The eyes, ears, nose, throat, teeth, and tongue were normal. There were no lesions on any of the mucous membranes. Liver and spleen were not palpable. The fundus extended 31.0 cm. above the symphysis. The fetus was in R.O.P. position, and the fetal heart was regular. The pelvis was quite adequate. There was a lesion that simulated an incipient paronychia on the middle finger of the right hand. There was marked pitting edema of both ankles, and the skin between the toes was moist and macerated. Neurologic examination was negative. There were no disturbances of sensation and no signs of latent tetany.

The Wassermann reaction was negative. The hemoglobin was 69 per cent (Sahli), the red count was 3,600,000, and the white count was 10,000. There were no bromides in the blood serum. Blood sugar was 70 mg. per cent and nonprotein nitrogen 22 mg. per cent. A catheter specimen of urine was negative.

The patient was seen by a dermatologist who made the diagnosis of dermatitis herpetiformis. The patient was kept in bed with a lighted cradle over her legs, and calomine lotion was liberally applied. There was little change in her condition and she required codeine. One per cent menthol in cold cream was applied with no relief. On July 12 the patient spontaneously went into labor. After nine hours and ten minutes, the cervix was fully dilated, and the head was 2 cm. below the spines. The fetal heart failed completely and forceps were applied. A right mesio-lateral episiotomy was done, and a male infant, weight 3,130 gm. and length 50 cm., was delivered. The child showed marked livid asphyxia. By means of tubs and carbon dioxide and oxygen inhalations the infant was resuscitated. Ten cubic centimeters of maternal blood were injected into his right buttock. At no time up to the present has the infant had any skin lesions. He has gained and been vigorous and normal in every way.

About twenty-four hours following delivery the skin lesions became much worse and an evening rise of temperature to 38° C. was noted. Fresh lesions appeared around her mouth, below her nostrils, and on her eyelids. The lesions on her trunk, thighs, and vulva coalesced and became very active. Great quantities of serum exuded from the broken vesicles and bullae that appeared in almost hourly crops. Macules that itched intensely first appeared and were rapidly replaced by blebs and vesicles. The itching was so intolerable that the patient would scratch herself in her sleep. The lesion of the nail bed on the right hand developed into a typical lesion which persisted throughout her stay and caused the nail to be distorted. Her white count rose to 16,000. Her urine was negative. Blood calcium was 8.0 mg. per cent, but there were no signs of latent tetany. Plasma proteins were 4.9 gm. (albumin 2.7, globulin 2.2) per cent.

Because of the similarity between the patient's condition and that of one suffering from a burn of a large area of the body surface, she was placed on sterile sheets under a lighted cradle, and 1 per cent aqueous gentian violet was applied periodically to her skin. All cultures of the lesions were negative. The gentian violet formed thick crusts which prevented the loss of much serum and relieved the itching in some degree. She was given three transfusions of from 350 to 500 c.c. of citrated blood. Wherever she was venesected, or a needle inserted in the skin,

Because of the failure of the fetal head to engage after an adequate modified trial of labor, a cesarean section was performed under gas, oxygen and ether anesthesia on the day of entry. The incision was made through that part of the abdominal wall which contained few lesions and the more involved portions were blocked off with sterile gauze covered with collodion. A healthy female infant, weight 2,760 gm., length 48.0 cm., with no skin lesions, was delivered. The placenta and cord showed no abnormalities.

The patient's postoperative course was febrile. Her pulse and temperature rose steadily until they reached 140 and 40.8° C., respectively, on the third postoperative day when she had two severe chills. Her abdomen was distended, tender, and silent. Her white count on the fourth day was 12,000. She became irrational and very restless. A diagnosis of peritonitis was made. The patient was Ochsnerized and was given a transfusion of 450 c.c. of citrated blood. Under this treatment she improved and her temperature and pulse became lower. A blood culture taken on the third postoperative day was reported negative. Fluids by mouth were started and she was given multiple small transfusions of citrated blood. Her temperature began to show a marked daily elevation and signs of wound sepsis became evident without definite localization. On the twentieth postoperative day about 400 c.c. of foul pus were evacuated from the deeper structures of the abdominal incision. From then on her improvement was rapid and she was discharged on the thirtieth postoperative day. At the time of discharge the skin lesions were markedly improved. The skin showed numerous small areas of brownish pigmentation where healing had occurred. A few crusted polymorphous lesions were present over the abdomen, thighs, and vulva.

The abdominal incision had healed well with the exception of a granulating area at the site of drainage. The uterus was slightly subinvolved, and there were tenderness and induration in the vaults. At no time during her course were there any mucous membrane involvement, diarrhea, or symptoms of latent tetany. No eosinophilia was ever demonstrated and repeated specimens of urine were negative.

The patient returned seven weeks after discharge from the hospital. The abdominal incision showed complete healing. The only evidence of skin involvement was the presence of a few brownish pigmented areas over the thighs and vulva. She had noted no fresh lesions of the skin and was in general excellent condition. The child had shown at no time any skin lesion and was also in excellent condition.

Because of the interest stimulated by the first patient, a much more satisfactory study was made of the second. She was a twenty-seven-year-old white married female who entered the hospital on July 7, 1935. She was due July 18. She complained of an itching rash of ten days' duration. It had first appeared as blisters on both sides of her nose and between her toes. Her chest, abdomen, thighs, vulval region, and shins soon were involved. She had tried to relieve the itching by breaking the vesicles by scratching or with a needle. As the rash became more generalized, marked ankle edema appeared. She had no symptoms of preeclamptic toxemia. Her habits were entirely unchanged and she denied the use of any drugs. She had no cramps, paresthesias, tetany or diarrhea. She had been treated prior to entry with some effervescent saline purgative.

The family history was irrelevant and there had been no nerve or skin diseases in her immediate family. She had had chickenpox, measles, and pertussis in childhood. She had never suffered from asthma, hay fever, urticaria, or other allergic manifestations. Menarche was at thirteen years. Her catamenia were normal and regular. She was supposed to have had a spontaneous abortion when a month pregnant in 1934. This abortion was not accompanied by any skin lesions.

On admission her temperature was 37.0° C., pulse 100, and respirations 17. The blood pressure was 136/76. She was a well-developed and well-nourished, young female in no obvious discomfort. Her hair was dry, brittle, and sparse, and she

face and there was so much local edema that she could barely talk or swallow. Cultures showed many colonies of beta streptococcus and *Hemolytic Staphylococcus aureus*. The patient was in the same precarious situation as one with a carbuncle of the upper lip or orbit. A special nurse kept continuous hot saline applications on the patient's face for four days. Fortunately, sinus thrombosis did not occur and the infection subsided on her face only to migrate and to appear under her breasts, in her axillae and on her shins and feet. She was given a series of six intramuscular injections of nonspecific foreign protein every other day. No local reactions appeared at the sites of injection. Liver extract in 2.0 c.c. doses was also given intramuscularly every other day from August 28 to December 15.

Following this period of acute infection there was a generalized regression of all infected lesions. Hot saline applications were continued wherever the purulent con-



Fig. 3.—A fresh crop of vesicles, and the scaling, chronically infected lesion on the face at the time autogenous vaccine therapy was started.

dition of the lesions seemed to indicate them. Her trunk was soon free from active lesions, and only pigmented areas remained. On September 18 she had shown marked improvement and her trunk was entirely covered with sound epidermis. Gentian violet applications were discontinued. She was washed with green soap and kept on sterile sheets under lighted cradles. The patient no longer complained of the intense itching, and, considering the severity of her symptoms, her condition was remarkably good. The eosinophilia and albuminuria persisted. On only one occasion was indican demonstrated in her urine. No eosinophiles were found in the blebs or vesicles.

On September 20, for the first time, typical lesions appeared on the mucous membranes of the hard palate. These disappeared in twenty-four hours. Throughout the rest of her stay she had transitory crops of vesicles on her oral mucosa that caused little discomfort. From September 21 to October 5 she was given eight sub-

a typical lesion appeared. Because of the supposed rôle of parathyroid hypofunction, or dysfunction, in disorders of this sort she was given 20 c.c. of cod liver oil and 3 gm. of calcium gluconate daily. She also received other supportive treatment in the form of a high vitamin diet and iron and ammonium citrate. Her blood calcium continued low. On July 29 it was 7.9 mg. per cent, and the phosphorus was 4.5 mg. per cent.

At no time were there any signs of puerperal infection. The uterus involuted rapidly and well. Her general condition was unchanged, and she was very uncomfortable because of the itching. New crops of lesions appeared frequently on the sites of former lesions where the skin was slightly pigmented. Three intramuscular injections of from 15 to 20 c.c. of the serum of normally pregnant women were given without any effect. Her pulse rarely went below 100, and she had occasional

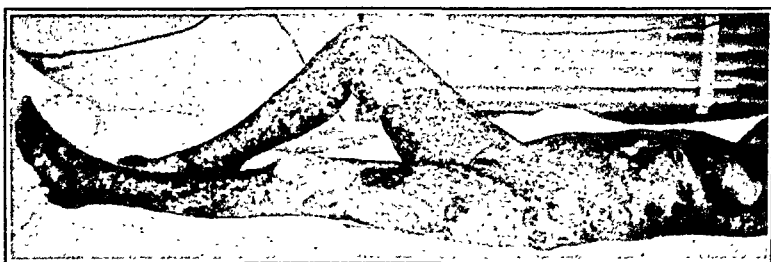


Fig. 1.—Appearance on Aug. 6, 1935, twenty-two days postpartum. The crusts formed by the gentian violet are very obvious.



Fig. 2.—A closer view of the right leg showing the polymorphous lesion, pigmentation, and crusts.

daily rises of temperature to the level of 39.4° C. About a month postpartum her urine began to show a persistent trace of albumin with numerous red and white cells in the sediment. At the same time a persistent eosinophilia, which at times was as high as 37 per cent, became manifest. No eosinophiles, however, were discovered in the blebs or bullae.

During the week of August 14 to 21 she seemed to improve and the lesions showed a general tendency to regress leaving the skin pigmented in brownish patches with irregular borders. She had a mild and persistent diarrhea which was not well controlled by either paregoric or bismuth subnitrate. On August 23, edema appeared around her eyes and fresh bullae appeared around her lips and eyes. The next day she had a chill and her temperature rose to 40.2° C. All the fresh skin lesions rapidly regressed after the chill. Frank pus appeared in all the involved areas of her

milliamperere minutes. After each exposure the regression of fresh lesions was remarkable. The patient would be encouraged and then lesions would appear elsewhere in the course of the subsequent twenty-four hours.

On November 14 she complained of a sore throat and of difficulty in talking. A laryngologist found ulcerations about 2 to 3 mm. in diameter on the epiglottis and left arytenoid. He suggested the possibility of a spirochetel or streptococcal infection, but it was felt that these were lesions similar to those on the oral mucosa. Shortly after this there was an exacerbation and new lesions appeared on her back involving the pigmented areas. Her temperature showed a marked daily rise, and she had a persistent tachycardia of 120 to 130. On November 24 she complained of a sore tongue and a typical lesion was discovered on it. Two days later the lesions on her tongue had disappeared without leaving a trace. Her rectum was examined by proctoscope for at least 18 cm. without difficulty, but no lesions were seen in rectal mucosa. Eosinophilia and albuminuria persisted.

From then on the improvement was gradual but steady. The lesions persisted especially around her mouth, in the left orbit, on both forearms, and on the dorsa of her feet. On January 15 ultraviolet treatment of lesions was started and was continued until February 3. The affected areas were exposed for two minutes at

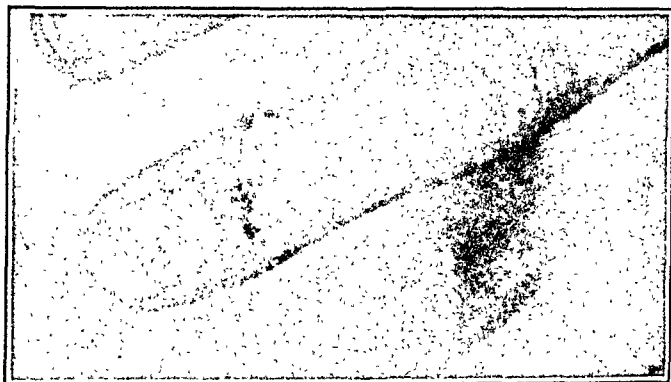


Fig. 5.—The lesion of the nail bed five months postpartum.

first and then for five minutes. By February 4 her face, trunk, and extremities were covered with sound skin pigmented a blotchy brown. The only areas which escaped pigmentation were the posterior surfaces of her thighs, buttocks, knees, elbows, palms, and soles. There was one small moist lesion barely a centimeter in diameter near her upper lip. She appeared in very good condition with little atrophy of her extremities after the long period of inactivity. Her temperature had been normal and her pulse 80 for fully a month. Her urine had become albumin free and the eosinophilia had dropped to 8 per cent. Blood calcium was 10.2 mg. per cent, phosphorus 5.7 mg. per cent, and plasma proteins 6.7 gm. per cent. (Albumin 3.7 gm. per cent, and globulin 3.0 gm. per cent.) A basal metabolic rate on discharge was minus 13 per cent. Plates of her skull and chest revealed no abnormality of the sella turcica or evidence of persistent enlargement of the thymus. Four days before discharge she commenced to have her first normal menstrual period since the time of delivery. At intervals of about twenty-eight days the patient had had a very slight bloody vaginal discharge for a few minutes the first two months after delivery. The other four months she had an absolute amenorrhea. Needless to say the baby was not allowed to nurse. The patient was discharged on the two hundred and sixth postpartum day. She returned for examination in six weeks. She had been taking viosterol and a high vitamin diet. The brown areas of pigmentation were blanching and presented a very mottled appearance. She had had

cutaneous injections of 100 c.c. of Ringer's solution in the sound skin of the buttocks. Each injection was followed by a generalized reaction, viz., chill and temperature elevation, but there was little local reaction. The fresh bullae and vesicles had a tendency to regress slightly after each reaction only in the uninfected areas.

Around her mouth, on her shins and the dorsa of her feet the lesions persisted apparently because they had become the sites of chronic infection. *Hemolytic Staphylococcus aureus* and beta streptococcus were again found on culture and stock vaccines were prepared. The condition seemed comparable to furunculosis. One-tenth of a cubic centimeter of each vaccine was injected intradermally. In twenty-



Fig. 4.—The residual pigmentation of the face following healing four months post-partum.

four hours the streptococcal vaccine had caused a wheal 2.5 cm. in diameter and the staphylococcal vaccine a wheal 1.5 cm. in diameter. About two days later typical polymorphous lesions developed at the sites of injection. Subcutaneous injections of the stock vaccines were made at four- or five-day intervals in doses increasing by 0.1 c.c. until 1 c.c. of each was given at a time. The site of each injection became the site of a typical lesion which went through all stages and was followed by the typical pigmentation of the skin.

On October 23, while still receiving the increasing doses of vaccine, the patient's left arm was given an exposure of 10 milliamperes minutes of unfiltered x-ray. This caused a dramatic regression of all fresh lesions in about four hours. Up to January 27 she received 27 exposures to the various affected areas of from 4 to 12

With the above convenient generalization it is possible to scrutinize the patients reported. The first patient had primarily involvement of the lower abdomen, thighs, and vulva with a polymorphous lesion, and, while under observation, no mucous membrane involvement. The second patient had a generalized rash of polymorphous character, intense itching, appearance of the rash in crops and was in excellent general condition despite the grave systemic manifestations. She also had involvement of mucous membranes, larynx, and nail bed. These symptoms have been reported in cases diagnosed both pemphigus, and dermatitis or impetigo herpetiformis, associated with pregnancy. The cultures of the lesions were at first sterile and the presence later of organisms was undoubtedly due to secondary infection. Eosinophiles have been reported in lesions of all three diseases, but none demonstrated in either patient. The second patient had diarrhea and Friedmann⁸ reported a case in which the skin manifestations associated with successive pregnancies were preceded by an attack of diarrhea. The patient also had prolonged amenorrhea postpartum in view of the fact that she was not allowed to lactate. Werther and Leszczynski^{5, 6} reported amenorrhea occurring with pemphigus associated with successive pregnancies for as long as two years. The persistent eosinophilia and the finding of red cells and albumin in the urine have been consistently reported by others. Other manifestations mentioned, which were not prominent in our patients, were loss of hair and involvement of the conjunctivae.

In neither patient were there any lesions on the children and in the second none appeared after injection of maternal blood intramuscularly. Blumenthal³ reported lesions on an infant similar to those of the mother in a patient diagnosed impetigo herpetiformis. The child was born a month prematurely and the lesions cleared spontaneously in fourteen days. The infant died later of intercurrent infection. The mother had received arsenic but none could be demonstrated in the infant's urine or meconium. Werther⁵ reported the case of a woman with pemphigus chronicus who had recurrent dermatoses with each pregnancy and who gave birth to a child covered with lesions which simulated the mother's but which disappeared in two weeks. This patient gave birth to a perfectly healthy infant in her next pregnancy. He also observed a thirty-seven-year-old woman with four previous normal pregnancies who developed pemphigus with her fifth pregnancy and gave birth to an infant covered with blisters filled with eosinophiles that disappeared in fourteen days. The mother died of an intercurrent staphylococcal infection, but the infant apparently flourished.

A most interesting finding in the second patient is the rather low blood calcium on entry. Modern German literature is replete with cases of hypoparathyroid tetany associated with impetigo herpetiformis.⁶⁻⁸ Unfortunately in most of the reports no figures are given for the blood calcium levels. Although our second patient had no signs of latent

another perfectly normal period. There was a 1 per cent eosinophilia and her urine was negative. Blood calcium was 9.7 mg. per cent and phosphorus was 3.5 mg. per cent.

On May 19, 1936, the patient again returned for routine postpartum checking. She was in excellent condition. The hemoglobin was 90 per cent (Sahli), the red blood cell count was 4,550,000 and the white blood cell count was 5,400. No eosinophiles were found on examination of the smear and the differential count was normal. The catheterized urine specimen was negative. Her skin over the neck, trunk, abdomen, vulva, arms, and legs still showed marked brownish pigmentation, but the skin of the face showed no pigmentation. Her menstrual periods had been normal and she had had no gastrointestinal or neurologic symptoms. The child was normal in all ways and had showed no skin rash.

COMMENT

The foregoing patients undoubtedly fall into the group of cases classed as dermatitis herpetiformis, impetigo herpetiformis or pemphigus vulgaris or chronicus associated with pregnancy. Hebra¹ first described "herpes impetiginiformis" in 1872. The vesicular lesions appeared in the region of the thighs and genitalia and were accompanied by grave systemic manifestations. Four of the five cases reported by him terminated fatally. Duhring² described dermatitis herpetiformis in 1884 and according to his original article, none of his cases occurred in pregnant women and none was fatal. The manifestations were protean, viz., macules, papules, vesicles, and bullae appearing successively in crops. The course of the disease was long and its manifestations rebellious to treatment. According to Sutton,¹⁵ in pemphigus the typical lesion is not polymorphous and the typical bullae appear on apparently sound skin. The mucous membranes are also more frequently involved. After reading a number of case reports and discussions, the distinctions between the three diseases appeared factitious to the authors. Some dermatologists are of the opinion that dermatitis herpetiformis and pemphigus vulgaris are identical, that lesions of the mucous membranes can occur in both and that no sharp distinction can be made between them clinically since the etiology is a mystery.¹³ Others feel that the diseases may undergo transitions from one form to the other. Other observers feel that there are three entities: dermatitis herpetiformis, pemphigus and transitional forms. The criteria for distinguishing between dermatitis herpetiformis and impetigo herpetiformis seem to be the tendency of the lesions to localize in the region of the genitalia and the graver systemic manifestations present in the latter.¹⁵ Modern authors report cases in men, children, nonpregnant women, and women past the menopause.^{6, 7} All authors agree that these symptom complexes are likely to run a long course uninfluenced by therapeutic measures and that spontaneous remissions are very likely to occur. A patient with these diseases can never be considered cured.¹⁵ There may be long periods of freedom from symptoms but exacerbations are notoriously likely to occur, especially with successive pregnancies in those patients in whom the original appearance was noted during pregnancy.

without any treatment. From the point of view of an obstetrician, it is important to know that these conditions are considered suitable indication for interrupting pregnancy and for avoiding pregnancy in the future, because of the notorious tendency to more severe exacerbations.^{8, 11} The prognosis for the fetus, if the disease occurs early in pregnancy, is poor. Intrauterine death, abortion and miscarriage are frequently reported.¹⁰ In later months premature labor commonly occurs.

Sedatives are necessary to control the itching. Any sort of local treatment that avoids secondary infection is indicated. Arsenic has been held in high favor at first in the form of Fowler's solution and later as sodium cacodylate, atoxyl or arsphenamine.^{3, 12, 15} The rationale of the use of arsenic has apparently been that it "improves the complexion in sublethal doses." Potassium iodide has been tried and reported to cause exacerbations. Quinine, plasmochin, germanin and mercury have been used. Mayer in 1910 suggested the injections of the serum of normal pregnant women. Gellhorn⁹ is about the only recent author to report favorable results. Horse serum and Ringer's solution have their advocates. Autogenous vaccines may be of some avail after the lesions have become secondarily infected. Our impression is that vaccination may have been of some value in controlling the infection but had no influence on the appearance of fresh lesions in the second patient reported. Because of the supposed hormonal origin of the symptom complex, all sorts of preparations from thyroid extracts to preparations of the ovaries, now known to be inactive, have been recommended. Jordan,¹² for example, recommends alternate treatment with arsenic and ovarian extracts. The administration of calcium to those with known low serum calcium would appear logical. Apparently the prolonged administration of calcium and cod liver oil raised the serum calcium from 8.0 mg. per cent to 10.0 mg. per cent but the course of the disease was not affected or mitigated. Most authors recommend the use of x-rays and certainly a transitory regression of lesions in a certain stage of development was obtained in our second patient. It must be kept in mind that when x-ray therapy was started a definite improvement had begun to occur in the second case reported and that the efficacy of that treatment cannot be accurately evaluated. Because of the possible rôle of the sympathetic system, irradiation of the spine has been suggested. Most authors agree that ultra-violet light may be somewhat helpful. In conclusion, to use the words of Duhring, it may be said that the symptom complex is very rebellious to treatment.

SUMMARY AND CONCLUSIONS

1. Two patients with dermatoses occurring during pregnancy are reported. Both occurred in primiparas near term and were characterized by polymorphous rash, itching, and the appearance of the rash in crops. In the first patient the lesions were primarily in the region of the geni-

tetany, 8.0 mg. was a low calcium level. Tetany is usually manifest at levels below 7.0 mg. per cent. Bohnstedt¹¹ has reported a case of impetigo herpetiformis associated with pregnancy and overt tetany in a woman who had had a thyroidectomy. Danisch⁷ has reported a fatal case of impetigo herpetiformis. The patient had had a subtotal thyroidectomy and the remaining apparently undisturbed parathyroids showed complete degeneration. Leszczynski⁶ has reported 4 cases of tetany and impetigo herpetiformis, three associated with pregnancy and one with prolonged amenorrhea. Schardorn⁸ first suggested an hormonal causal factor, dysfunction of the parathyroids. Most cases of impetigo herpetiformis are supposed to have occurred in the spring when most cases of tetany, or tetany associated with pregnancy, have been reported. Friedmann⁸ suggested the possibility of a toxin of pregnancy depressing the function of the parathyroids. Bohnstedt¹¹ felt that the pregnancy was incidental because of the usual exacerbation of symptoms postpartum. The prematurely delivered fetus in his case had defective calcification of the bones. Danisch⁷ and Leszczynski⁶ suggest the theory that impetigo herpetiformis is due to a dysfunction of the sympathetic nervous system secondary to a disturbance in available ionized calcium. Cataract, changes in the hair and nails and night blindness all are known to occur with tetany and impetigo herpetiformis. Klopstock⁴ in writing of pemphigus vulgaris associated with pregnancy attributes the blister formation to the changes in permeability brought about by the disturbance of the equilibrium of ions of the serum through some detrimental influence on the sympathetic nervous system. The blood calcium, apparently one determination, in the case reported was 9.4 mg. per cent; the blood was taken after delivery. Osteomalacia has been reported as occurring with impetigo herpetiformis.⁵ Persistent thymus and changes of the hypophysis have accompanied the disease. Because of the similar embryologic origin of the parathyroids and thymus, it has been attractive to associate them in an explanation of the etiology. There was no evidence of enlargement of the thymus or pituitary in the case reported.

Hebra¹ considered the disease due to a fetal toxin. Howard¹⁰ suggested damage to the vasomotor nerves by toxins or ferments from the chorionic epithelium. The placentas are supposed to show infarcts but in both of our patients no abnormalities were noted. Gellhorn⁹ also assumed the cause to be some toxin connected with the pregnant state. Schreiner¹³ attempted to explain the manifestations as due to sensitivity to iodine, and Werther as of allergic origin. Since the etiology of the symptom complex is so obscure, the means of treatment are very unsatisfactory. Most authors admit that treatment seems to influence the course of the disease very little and that prevention of secondary infection and supportive treatment are all that can be accomplished. Cases have been reported that dropped treatment and soon became symptom-free. Friedmann⁸ admitted that healing would probably have occurred in his case

A CONSIDERATION OF LUMBOSACRAL SPINA BIFIDA OCCULTA WITH SPECIAL REFERENCE TO UTERINE PROLAPSE*

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FOR several years I have been conscious of the fact that certain conditions encountered in the practice of gynecology are sometimes associated with occult spina bifida. Among them are bladder dysfunction, uterine prolapse in nulliparas, low back pain, anal sphincter weakness, and saddle anesthesia. An attempt to learn more about the rôle of the spinal deformity in bladder dysfunction and uterine prolapse has revealed widely different opinions about nearly every phase of spina bifida occulta but very few contributions dealing with genital prolapse. Therefore, a collective abstract of some of the literature together with certain personal observations are presented, with the thought that they are important enough to keep a pelvic surgeon more mindful of the posterior part of the pelvic girdle.

I. REVIEW OF LITERATURE

Historical.—The earliest recorded case is that of Athol, 1857, entitled "Fatty Tumor from the Sacrum of a Child Connected with the Spinal Membranes." Virchow was the first to use the term "spina bifida occulta," when in 1875 he reported the case of Miss Bell Carter of Blue Bank, Kentucky, who appeared in museums as "The Lady with a Horse's Mane" and proved to have the hidden spine defect in the upper dorsal vertebrae. Von Recklinghausen, 1886, in a classical paper described the pathology and gave the name "membrana reunions posterior" to the connective tissue membrane that fills out the patency between the rudimentary neural arches. Alfred Fuels, 1909, drew attention to the clinical entity that he found with an open sacral canal in all gradations down to a pathologic form of the sacral hiatus and coined the term "myelodysplasia" for the symptom complex he described; weakness of the sphincters, especially nocturnal enuresis persisting after puberty; syndactylis musually involving the second and third toes; disturbance of sensation, chiefly temperature sensation in the feet and toes; anomalies of cutaneous and tendon reflexes in the abdomen and lower limbs; club feet, sometimes with peroneal weakness; trophic and vasomotor disturbances in the toes.

Fuels is often quoted, sometimes incorrectly, and the term myelodysplasia was adopted by Spiller and others. Gould's medical dictionary gives occult spina bifida as the synonym of myelodysplasia. Since the term implies a cord defect that does not always exist, it may have retarded progress in surgical treatment of the lesion. Brickner, in 1918, found only 12 operations reported in the literature and added five of his own. H. O. Mertz, of Indiana, 1933, found in the literature 79 laminectomies for occult spina bifida performed because of nerve control disturbance of the lower urinary tract in which the reports warranted conclusions as to results.

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talia, and in the second, their distribution was generalized. In the first patient, cesarean section was done because of failure of the head to engage after an adequate modified trial of labor. The postoperative course was complicated by peritonitis and wound sepsis. No special treatment was given for the skin lesions.

The second patient ran a course of 206 days following delivery. The loss of serum proteins due to involvement of large skin areas necessitated treatment as a burn. Secondary infection greatly complicated the course. Grave systemic manifestations were present together with eosinophilia, albuminuria, hematuria, diarrhea, amenorrhea, mucous membrane, and nail bed involvement. The serum calcium was low before delivery but tetany was never demonstrated. Calcium, cod liver oil, liver extract, the serum of pregnant women, Ringer's solution, nonspecific foreign protein, autogenous vaccine, x-rays, and ultraviolet light were all used in treatment. The disease probably ran a course uninfluenced by these measures and the most that can be said to have been accomplished was the prevention of loss of serum proteins and the control of secondary infection.

2. Impetigo herpetiformis, dermatitis herpetiformis, and pemphigus chronicus, or vulgaris, are, judging from a review of a number of case reports, similar symptom complexes. Similar manifestations are reported with all. Unfortunately, most case reports are deficient in studies of blood chemistry. The dermatoses recur with subsequent pregnancies. Amenorrhea is a frequent sequel.

3. The etiologic factors are not clear. Parathyroid dysfunction may play some part. Striking cases of impetigo herpetiformis associated with tetany have been reported.

4. Treatment probably influences the disease very little. Efforts should be directed toward maintaining the general condition of the patient and toward the prevention and control of secondary infection. In pregnancy the disease is an indication for termination and the prevention of future pregnancies. If the disease manifests itself early in pregnancy the outlook for the fetus is not good.

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Since the spine grows faster than the cauda equina, symptoms due to stretching of the roots may not appear until adolescence or adult life. The myofibrolipoma, also called a teratoma, may grow at any time and cause pressure symptoms. Trauma may aggravate latent symptoms.

X-ray Diagnosis.—The x-ray diagnosis of spina bifida occulta has been found accurate as a rule. It has been noted, however, that calcification of the membrana reuniens posterior has led to faulty interpretation. There is a healed form of occult spina bifida, not demonstrable by x-ray, in which external signs and nerve changes are present. Operators have commented upon the discrepancy between the x-ray findings and the true pathologic condition in young children. The difficulty of establishing the diagnosis of a neurologic lesion in connection with the bony defect has led to the injection of lipiodol into the spinal canal. This procedure is not without its dangers and has not become as popular in this country as it is in France.

Clinical Signs and Symptoms.—Of the local signs hypertrichosis is the most striking, but occurs in only 4 per cent of cases. It is congenital but increases at puberty. Fovea sacralis, one or two sacral dimples, persisting after the twelfth year, signifies a developmental sacral defect. It was found by Cramer in 40 per cent of 200 infants. Scars, striae, naevi are occasionally found. A subcutaneous lipoma or hemangioma may be present. The local signs are usually absent and any of them can occur without occult spina bifida (Winkler, W.). The spinal cleft may be palpated if it is wide enough. Pressure over the cleft caused a desire to void in one of my patients.

The bifid neural arch weakens the spinal column by impairing ligamentous attachments and predisposes it to strains and sprains. The weakness may be dormant until put to test by severe stress or trauma. Dr. W. S. Newcomet x-rayed a large number of men in a military training camp who complained of disabling low back pain, and he found an astonishing incidence of occult spina bifida. Halstead made the same observation in another camp.

Peripheral Symptoms.—The neurologic symptoms consist of motor, sensory, and trophic disturbances and may be absent or occur singly or in groups. They may be indistinguishable from symptoms produced by other lesions, and even if found coexisting with the spine defect there may be no causal relationship. Saddle back anesthesia may be present involving the buttock, perineum, and posterior half of the vulva. Other deformities may be present either as a result of the nerve lesion or independently. The commonest deformity, clubfoot, is ascribed to progressive paralysis and most often is of the clawfoot type (A. Steindler). It is estimated that spina bifida occulta is present in 60 per cent of persons with clubfoot. Flexion contracture of the knee and dislocation of the hip are reported (G. Pieri and R. S. Smith).

Visceral Symptoms.—(a) *Anorectal signs* include relaxed sphincter ani, sometimes with incontinence, sometimes with prolapse of the rectal mucosa; loss of anal reflex; loss of the normal retraction of the anal area when the levator ani muscles are paralyzed (Coughlin).

(b) *Urinary Signs and Symptoms:* Enuresis is almost universally regarded a prominent symptom. The theory is that the dysfunction is primarily irritative. Constant irritation affects the vesical center in the cord and so alters its action that during sleep when there is no psychic control the bladder automatically empties.

Peritz said that 68 per cent of adults with nocturnal enuresis have spina bifida occulta. On the other hand, West found it no more frequent in 81 adult bed wetters than in 100 controls. Without doubt, functional incontinence, not merely nocturnal, is the commonest urinary symptom. Next in frequency is partial retention with or without overflow. Acute retention is rare. Dilatation of the ureters and renal pelves without obstruction occurs in children probably as the result of defective innerva-

Over half were successful and the majority of the remainder were ameliorating. There was one death. Mertz recorded six operations. These operative results show that a congenital cord lesion is not present as frequently as was formerly believed.

Definition.—Posterior spina bifida occulta may be defined as a developmental deformity in which there is a cleft in the laminae of one or more vertebrae but no external sac. It is a rudimentary form of spina bifida (merorrhachisis). The laminae may be absent, or gape, or pass each other without fusing. In minor degrees of the defect the laminae meet except for a thin wedge of cartilage or there is a bifid spinous process. It occurs most frequently in the lumbosacral region where the vast majority of spine anomalies are located. Bony closure of the posterior vertebral arches begins in the lumbar region and proceeds upward and downward. Ossification begins at birth or earlier and the spinous processes of the lumbar and first sacral vertebrae are ossified by the third year, while ossification of the fourth sacral is delayed until the seventh year. The appearance of spina bifida occulta is a normal finding in young children and occurs in 91 per cent from one to two years of age (Hintze).

Incidence.—Theodora Wheeler studied a thousand consecutive x-ray plates of the lumbar region in white adults over eighteen years of age at Johns Hopkins Hospital. She found incomplete closure of the last lumbar arch in 2.3 per cent, the incidence in males and females being about the same. She found incomplete closure of the first sacral arch in 13 per cent, but said, "one must choose a rather arbitrary standard of what constitutes a defective first sacral arch, since transitions from a fully formed one to an incomplete one are gradual." She collected several large series from the literature and calculated the entire sacrum was open in 2.89 per cent. Willis studied 1,400 skeletons and noted a bifid neural arch in 1.2 per cent of the last lumbar vertebrae. He regards bifid neural arch as a normal finding in the lower sacral segments and noted its great frequency in the first sacral. Schmorl and Junghans, in their x-ray study of 10,000 spines, are in accord with writers who place the incidence of the anomaly at from 15 to 20 per cent. Those who report an incidence of 35 per cent must include cases in which the sacral hiatus reaches a higher level than they consider normal. Radlauer studied 500 sacra in various races and found that closure of the hiatus sacralis occurred, over the third arch and between the third and fourth in 27.4 per cent, over the fourth arch and between the fourth and fifth in 45.6 per cent, and over the fifth arch in 14 per cent.

This wide variation in opinions as to what x-ray findings are to be interpreted as occult spina bifida no doubt explains the contradictory views of those who think it is never important clinically and those who find it associated with symptoms in nearly every case. If we discard minor posterior fusion defects of the first sacral arch and all varieties of sacral hiatus, there will remain an incidence of at least 4 per cent in adult women that must be considered definite cases of occult spina bifida. I believe that, in addition to these, anomalies of the lower sacral segments deserve further study, since the sacral plexus is composed of nerves emerging through the second, third, and fourth sacral foramina and can readily be involved, not only at the lumbosacral junction but also low in the sacral canal.

Pathology.—When the cord is primarily involved the picture is akin to syringomyelia. At operation and autopsy the usual findings have been: (1) Closure of the cleft by a tough membrane adherent to the overlying skin or nonencapsulated fat and connective tissue; (2) a myofibrolipoma extending through the cleft and into the bony canal disturbing and compressing the cord and its roots; (3) perforation of the membrane by a dense band attached to the subcutaneous tissues externally and compressing the cord structures internally.

limited to the sacral hiatus, and they are not included. I have previously reported a personal failure to cure incontinence by the Kelly operation in a nullipara with occult spina bifida.

COMMENT

There is ample evidence in the literature to show that occult spina bifida may cause motor and sensory disturbance in the sacral plexus.

Symptoms due to involvement of the sacral plexus should be the most common, since it is involved by fusion defects at the lower as well as the higher levels of the lumbosacral region.

The emphasis usually placed upon nocturnal enuresis, a rare complaint in gynecologic practice, may properly be directed to other symptoms of bladder dysfunction in women.

Weakness of the pelvic floor and relaxed sphincters are associated with occult spina bifida more often than is indicated by current gynecologic publications.

These symptoms may be latent or absent until adult life, and then be considered as entirely due to injuries of childbirth.

The vaginal plastic surgeon should think of occult spina bifida in terms of innervation of the skin, muscles, and connective tissues of the pelvic floor, not merely as it may be related to virginal uterine prolapse.

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DISCUSSION

DR. SAMUEL B. HADDEN.—This subject is one that has been recently receiving attention that will result in a more clear understanding of the problem of spina bifida occulta.

The common complaints of spina bifida occulta are mainly those of bladder dysfunction, plus a sense of disturbance in the sacral distribution. Those symptoms are very much the same as those of cord tumor. In reality, spina bifida occulta is

tion of the pelvic ureter (Mertz). In severe cases a "Cord" bladder has been found. Sometimes there is anesthesia of the urethra (Findlay).

(c) *Uterine Prolapse*: It has been stated that uterine prolapse in nulliparas, in the majority if not all cases, is due to the existence of an unrecognized occult spina bifida which involves the fourth sacral nerve with consequent paralysis of the levator ani muscles and shows a pronounced tendency to recurrence after operation (Sturmdorf). Ebeler x-rayed 28 parous women with uterovaginal prolapse and found 23 of them to have occult spina bifida as compared with 28 parous women without prolapse of whom three had this defect. He gave no details of these remarkable findings (Ebeler and Duncker). Palmer Findley in 1917 called attention to this observation and to the fact that prolapse in the newborn was nearly always associated with spina bifida vera. He concluded, with other writers, that defective innervation of both the muscular and connective tissues is a causative factor in congenital uterine prolapse.

II. PERSONAL OBSERVATIONS

In my follow-up clinic I found 3 multiparas with early recurrence after operation for procidentia. All three had definite spina bifida occulta. I then decided to repeat Ebeler's study and had x-rays made in 25 other parous women operated upon for uterovaginal prolapse. Only one of the 25 showed a definite spina bifida occulta. This patient was particularly traced because I remembered that she had the combination of procidentia and postoperative foot drop in a congenitally deformed limb which proved to be dislocation of the hip. She still has a good result nine years after vaginal hysterectomy. I have had two other patients with postoperative foot drop. Both followed vaginal operations for prolapse. X-ray was negative in one case, diagnosed hysteria; the other has not been traced. My findings were not striking like those of Ebeler, quoted above, but they are at least suggestive that occult spina bifida may be a more frequent cause of recurrence of prolapse in multiparas than is generally recognized. Consideration of foot drop calls attention to Spiller's warning that extreme flexion of the trunk on the thighs may overstretch the caudal roots and produce paralysis of the legs and bladder. Conversely, overflexion of the thighs in the lithotomy position may stretch these roots, especially if already put on stretch by adhesions to the sacral canal, as occurs in occult spina bifida.

For comparison with the 25 x-ray films, I looked up the films of 25 women recently examined for kidney lesions and again found only one with occult spina bifida of the same severe degree. This patient had a stricture of the pelvic ureter, similar to one formerly found in a young woman with the spine defect.

I have had x-rays taken in several women with unexplained bladder dysfunction, usually manifested by incomplete control or residual urine, and have found five of them to have definite spina bifida occulta. Two other bladder cases were reported by radiologists elsewhere to have occult spina bifida but the films were found to show an anomaly

minutes. Pitocin caused an increase of only 5 mm., returning to the normal in five minutes. They made no studies of the water balance and the observations on the blood pressure changes were inadequate.

Chipman and Dieckmann each have stated that the use of pituitrin in the induction of labor in preeclamptic patients has occasionally seemed to be the cause of the onset of convulsions. Eclampsia, of course, occurs most frequently during labor, and the irritating effects of the uterine contractions may have been the cause of the onset of the convulsions rather than the pressor and antidiuretic action of the pituitrin.

METHOD

Catheters were inserted into the bladders of normal and toxemic, pregnant, parturient, and puerperal women for the period of study. Water was given by mouth in amounts varying from 150 to 250 c.c. per hour. Urine specimens were collected every hour. After a satisfactory volume of urine had been obtained, one-half to two minims of pituitrin, or one of its fractions, were injected subcutaneously in the pregnant patients and intravenously in those in the puerperium. Blood pressure readings were taken before the injection until they were constant, and then every two minutes for a period of ten minutes following the injection. The blood pressure either returned quickly to normal or it remained increased for hours. Sixteen normal pregnant women, 12 patients with vascular-renal disease in pregnancy and 19 toxemic patients have been studied.

RESULTS

Normal Pregnancy.—The volume of urine excreted per hour was not diminished during labor. The injection of pituitrin or pitressin produced a marked decrease

TABLE I

SUBSTANCE INJECTED	NUMBER OF PATIENTS	VOLUME OF URINE PER HOUR				BLOOD PRESSURE INCREASE IN MM. OF HG	
		HOURS BEFORE INJECTION		HOURS AFTER INJECTION			
		2	1	1	2		
A. Normal Pregnancy							
Pituitrin	15	Average	153	149	77	77	11
		Range	50-219	30-300	10-180	5-198	0 to 20
Pitressin	6	Average	165	169	127	113	4.8
		Range	110-195	114-210	65-165	62-170	0 to 8
Pitocin	5	Average	159	188	128	122	2.5
		Range	136-180	168-210	96-160	92-152	0 to 4
B. Vascular-Renal Disease in Pregnancy							
Pituitrin	12	Average	176	179	119	110	7.7
		Range	122-230	120-250	60-195	65-166	-10 to 18
Pitressin	6	Average	186	180	130	136	6.8
		Range	166-204	152-210	64-160	90-166	0 to 8
Pitocin	9	Average	196	192	129	145	6.8
		Range	154-224	152-218	82-172	44-180	-2 to 14
C. Preeclampsia							
Pituitrin	19	Average	150	135	49	60	51
		Range	17-305	18-300	0-100	0-300	28 to 80
Pitressin	4	Average	92	112	46	72	23
		Range	46-128	32-183	16-70	24-110	10 to 44
Pitocin	5	Average	149	142	53	75	20
		Range	96-210	82-198	32-112	15-192	12 to 28

a product of spinal tumor in that the symptoms are the result of involvement of the fibers after they have left the cortex. At the present time, I feel the problem of what constitutes spina bifida occulta and the importance of x-ray findings is in very much the same situation as was the problem of head injury when we paid so much attention to the x-ray findings. I do not believe the x-ray findings in themselves are of particular importance.

The voluntary innervation of the pelvic muscles is of course from the lower sacral routes, but in addition they must receive definite sympathetic innervation. This sympathetic innervation comes off at a much higher level than would be involved in an ordinary spina bifida occulta, although lesions in the sacral levels could cause involvement of the parasympathetic systems.

Very recently some splendid work has been done by Dr. Lanworthy on the control of the bladder, and by his systematic studies, he has aided considerably in adding to the knowledge of spina bifida occulta.

In conclusion, I repeat that many of the symptoms of spina bifida occulta are nothing more than symptoms of a cord tumor. The problem is one which should receive more attention and lead to more cooperation between gynecologists and neurologists.

VASCULAR-RENAL EFFECTS OF POSTERIOR PITUITARY EXTRACTS IN PREGNANT WOMEN*

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THE parenteral or intranasal administration of extracts of the posterior lobe of the pituitary gland produces a decrease in the volume of the urine, an increase in the concentration of the urinary chloride, and little or no rise in the blood pressure of nonpregnant individuals. The duration of these changes varies with the amount of extract administered, but the magnitude of the response seems to bear no relation to the size of the dose. Pituitrin given to certain patients with toxemia of pregnancy produced responses similar to those described above with but one exception, namely, a marked increase in the blood pressure. This susceptibility to pituitrin was noted with great constancy in typical preeclamptic and eclamptic patients; it, therefore, appeared to offer a means of differentiating these patients from the pregnant women with primary or secondary hypertension.

Kamm and his coworkers have been able to separate two fractions from the posterior lobe of the pituitary gland, pitressin and pitocin. Pitressin is composed of the pressor and antidiuretic components, while pitocin contains the oxytocic principle. Each preparation has a minute amount of the other.

Ward, Lyon and Bemis compared the action of pituitrin, pitressin, and pitocin on pregnant women. They stated that pitressin and pituitrin produced an increase in the systolic blood pressure of 17 and 10 mm., respectively, which lasted for fifteen

*Read at a meeting of the Chicago Gynecological Society, May 8, 1936.

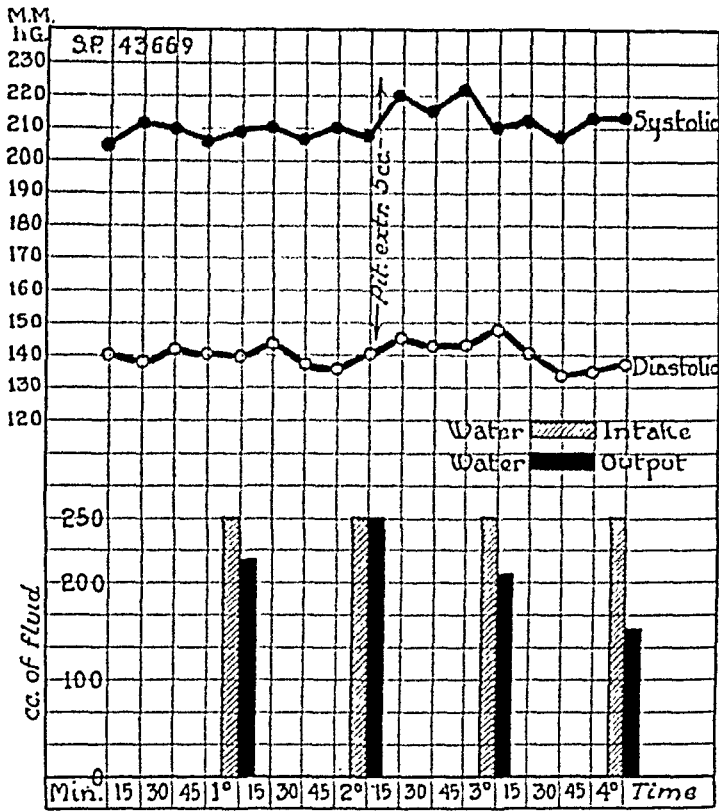


Fig. 2.—Vascular-renal disease (essential hypertension) in pregnancy. Pituitrin has no appreciable effect on blood pressure.

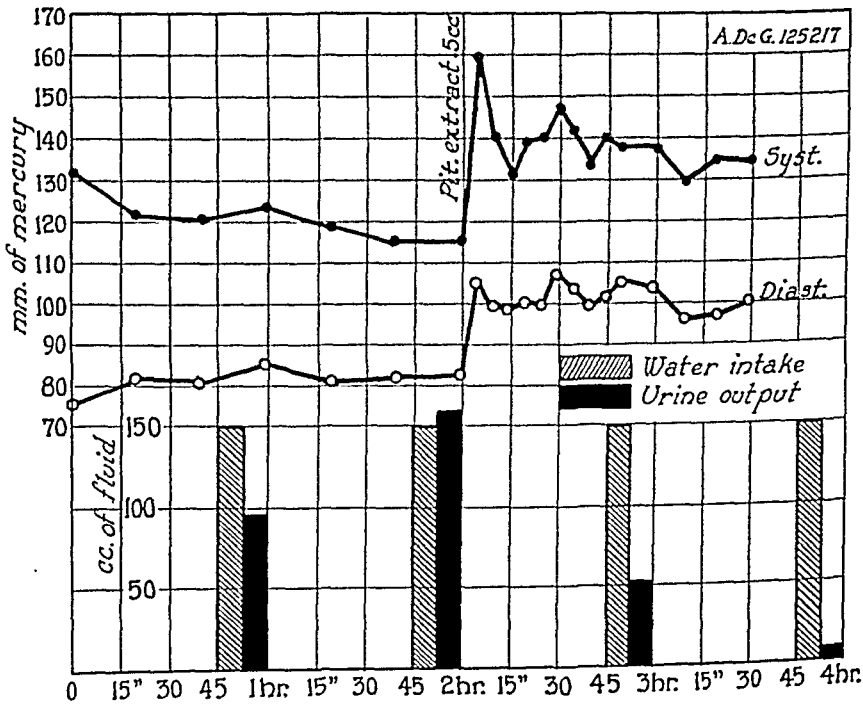


Fig. 3.—Preeclampsia. Pituitrin causes marked increase in both systolic and diastolic blood pressure and also an oliguria.

in the volume of urine and slight to moderate elevations in the blood pressure. No significant differences were noted for the three substances, although pituitrin, as a rule, gave a more marked increase in the blood pressure. Injections of pitocin did not have as great effect on the urine volume and blood pressure as the other two substances. The average figures are given in Table IA. A typical case is illustrated in Fig. 1.

Vascular-Renal Disease in Pregnancy.—This group is composed of patients who are commonly designated by the obstetrician as having "chronic nephritis." Other terms used are "recurrent toxemia of pregnancy," "latent nephritis," "occult nephritis," etc. The important abnormal finding is a hypertension. Albuminuria frequently occurs near term. The renal function is usually at the lower limits of normal. Ophthalmoscopic examination is of value only if it shows abnormal changes. Usually the disease has been of relatively short duration and little, if any, pathology is present in the arterioles of the eyes or skeletal muscles and no cardiac hypertrophy

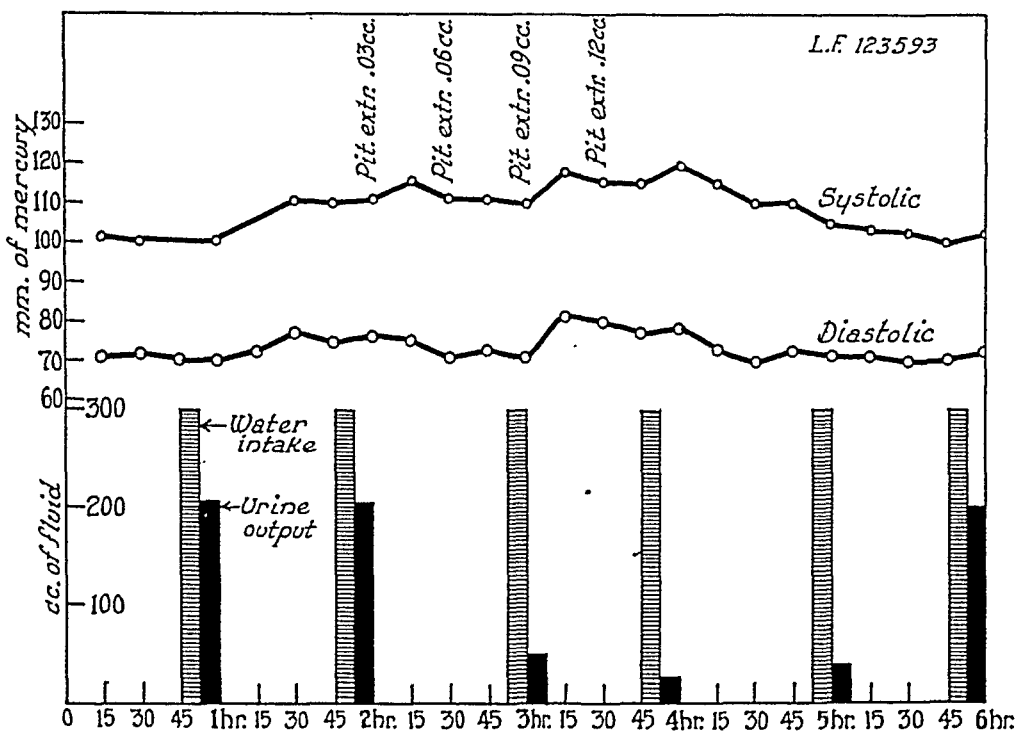


Fig. 1.—Normal pregnancy. Pituitrin causes marked oliguria but no increase in blood pressure.

is ordinarily demonstrable. The hypertension may have been present before pregnancy occurred or it may have been caused by the pregnancy. A small majority of pregnant women have renal impairment which is due either to a chronic glomerulonephritis, nephrosclerosis, or eclampsia. The responses obtained with the three substances are similar to those found in normal pregnancy. The average figures are listed in Table IB. A typical case is illustrated in Fig. 2.

Preeclampsia.—This condition is characterized by the appearance of edema, albuminuria, and hypertension in pregnant women who had not shown these signs previously. Various cerebral and visual symptoms, which may be the result of edema of the brain, gastrointestinal symptoms, and an oliguria or anuria usually occur just before the onset of convulsions and coma. Injection of pituitrin caused a very abrupt and marked increase in both the systolic and diastolic blood pressure and a marked decrease in the volume of urine. No significant difference was noted with the use of pitressin or pitocin, excepting that the increase in blood pressures was less marked.

unable to demonstrate the pressor and antidiuretic substances in the blood obtained from preeclamptic and eclamptic patients. Thus the work of Anselmino and Hoffman remains unconfirmed. Their conclusions were apparently based on too few controls and an insufficient number of experiments.

The results obtained in this study have a double implication: (1) The injection of pituitrin per se may be dangerous in toxemic patients even in small amounts. There is some indication that pitocin is more desirable where the injection of a pituitary extract is indicated; (2) pituitary extract in minute doses offers a good test in differentiating preeclampsia from vascular-renal disease in pregnancy.

In a previous paper the authors emphasized the value of the cold pressor test in pregnancy. In that study 190 patients (300 to date) were observed. Patients with vascular-renal disease in pregnancy gave marked pressor responses with ice water stimulation, whereas the preeclamptic patients gave only moderate and variable pressor responses.

Thus, we have a double check for differentiating the two types of conditions in pregnancy, namely, the administration of small doses of pituitrin to indicate which patients are preeclamptic, and the cold pressor test to indicate which patients belong to the vascular-renal group.

The fact that an injection of pituitrin may produce an oliguria, rise in blood pressure, and other symptoms makes its administration undesirable in preeclamptic patients. The use of ergonovine after delivery would seem preferable. Adair, Davis and coworkers stated, "We reached the tentative conclusion that the administration of ergotocin (ergonovine) in therapeutic doses has little or no effect on the blood pressure curve of patients with or without hypertension. We also believe that there is no effect on urinary output."

CONCLUSIONS

1. The volume of urine is not diminished during labor in normal pregnant women if the fluid intake is adequate.

2. It is, however, decreased during labor in preeclampsia or eclampsia, and the forcing of fluids may produce undesirable and occasionally dangerous symptoms and signs.

3. The parenteral injection of extracts of the posterior lobe of the pituitary gland produced the following changes:

a. A decrease in the volume of urine, an increase in the chloride concentration, and an average rise in the systolic blood pressure of 11 mm. Hg in normal pregnant, parturient, and puerperal women. Similar changes occurred in the vascular-renal group.

b. A markedly decreased volume of urine, an increase in the chloride concentration, and an average rise in the systolic blood pressure of 51 mm. Hg in preeclamptic patients.

The oliguria became so marked in one patient following the injection of pituitrin that an acute pulmonary edema was produced. In another patient there was an abrupt and marked rise in the blood pressure, which may have been a factor in causing the partial abruptio placentae.

Average figures are listed in Table IC. A typical case is illustrated by Fig. 3.

The specimens of urine were analyzed for chloride and nonprotein nitrogen, and the specific gravities (gravimetric method) were also determined. The urine obtained after the injection of pituitrin or either of the fractions usually showed an increased concentration of chloride. There was little or no alteration of the non-protein nitrogen concentration. Naturally, the specific gravity would be increased if the chloride concentration was increased. No correlation could be demonstrated between the degree of decrease in the volume of the urine and the increase in the chloride concentration.

DISCUSSION

Anselmino, Hoffman and Kennedy reported that they had demonstrated an excessive amount of the antidiuretic and pressor principles of the posterior pituitary gland in the blood of patients with toxic albuminuria of pregnancy or eclampsia. They stated "full agreement was established between the most important individual symptoms and experimentally reproducible actions of the autacid; these included water retention through diuresis inhibition, rise in blood pressure, capillary spasm, coma and fits, lung edema, the lessening of galvanic irritability, certain ionic movements from blood to tissues, and the controlling effect obtained by certain definite narcotics and hypnotics. Quantitative estimations of the autacid ran parallel to the severity of the symptoms. The hypothesis is advanced that toxic albuminuria of pregnancy and eclampsia are endocrine disturbances probably of a pluriglandular nature, but in which great overproduction of the hormones of the posterior pituitary dominates the picture."

Our work demonstrates that the preeclamptic patient reacts markedly to injections of the posterior pituitary gland, as evidenced by the oliguria, increase in blood pressure and occasional appearance of the characteristic cerebral and visual symptoms and signs. The increase in blood pressure is much greater in preeclampsia than it is in normal pregnancy or vascular-renal disease.

The fact that injections of pituitrin act as they do in preeclamptic patients indicates the possibility that the posterior lobe of the pituitary gland may in some way be associated with the disease. Too much secretion may be produced, there may be some defect in its neutralization, or the individual may be unduly susceptible to its action. The rapid amelioration and occasional disappearance of all symptoms and signs within a period of two or three days in both preeclampsia and eclampsia indicate that if there was any disturbance of the pituitary gland, it was a functional one and not an organic change in structure.

Our data would seem to lend strong support to Anselmino and Hoffman's work. However, Byrom and Wilson, Theobald, Page (assisted by Anselmino), and Hurwitz and Bullock, working independently, were

one generally employs an incision large enough, even though it extends well above the umbilicus, in order to liberate the tumors.

To obviate the blood loss entailed by the preliminary morecellation as previously practiced, at the same time conserving the abdominal wall, I have in the past two years employed in six cases the method presently to be described.

PROCEDURE

The incision is entirely subumbilical. In four of the six cases, although the fibroids reached well up into the epigastric space, the incision was below the umbilicus. The vesicouterine peritoneum is picked up and incised to extend

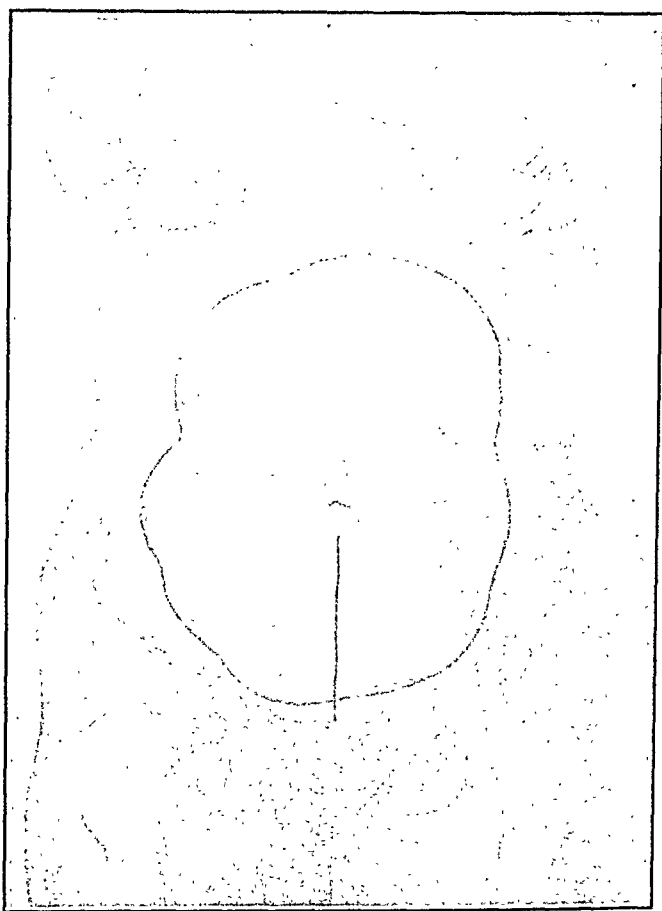


Fig. 1.—Outline of large myomatous uterus reaching the epigastric space in relation to the median suprapubic incision.

to each round ligament which is divided between two ligatures (Fig. 2). If the adnexa are to be removed they are ligated and severed from the infundibulopelvic ligament. If they are to be retained they are clamped off at the uterine attachment and secured by ligatures (Fig. 3). The age of the patient and the condition of the adnexa determine the one or the other step.

The uterine vessels are ligated on both sides, or first on one side, followed by amputation of the cervix. Then the vessels of the other side may be grasped and ligated (Fig. 4). This step is quite the same as that employed by Kelly, Doyen and others, except that the myomatous uterus by the present method is allowed to remain within the abdomen for a few minutes after it is completely severed from its cervical attachment and blood supply. When the tumors are mostly situated

4. The cold pressor test is emphasized as a method to differentiate the vascular-renal group from the preeclamptic group.

5. The dangers of pituitrin in the preeclamptic group are made apparent, but its value as a test is emphasized.

6. Pitocin does not produce as marked an increase in blood pressure as pituitrin, hence, pitocin is preferable to pituitrin for the induction of labor in toxemic patients.

7. Large doses of none of the extracts of the posterior lobe of the pituitary should be given routinely to toxemic patients after delivery. If bleeding is anticipated or occurs, ergonovine is probably preferable.

8. Our conclusions are based on a comparatively small number of patients, but the fact that the "pituitrin test" may aid in differentiating preeclampsia from other toxemias of pregnancy warrants further investigation to definitely determine its value. Furthermore, its use early in pregnancy may enable us to detect the patients who may subsequently develop preeclampsia.

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"RETROGRADE" ABDOMINAL HYSTERECTOMY WITH AVASCULAR MORCELLATION FOR LARGE FIBROIDS

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THE removal of a fibromyomatous uterus by morcellation is not a new procedure. It was employed even before the modern method of hysterectomy was fully developed. Morcellation in combination with the standard technic through a relatively small incision has also been practiced, particularly by European gynecologists. The tumor mass was reduced in size until the remnant of the tumor-bearing uterus could be delivered through the abdominal wound after which it was removed in the typical manner.

The advantage which this technic offered the patient, by conserving as much of the abdominal wall as possible, was, however, offset by the considerable amount of blood lost during the process of cutting up the tumor masses. The operation has therefore been abandoned and now



Fig. 4.—The cervix stump sutured and peritonealized together with the adnexal and round ligament stumps.

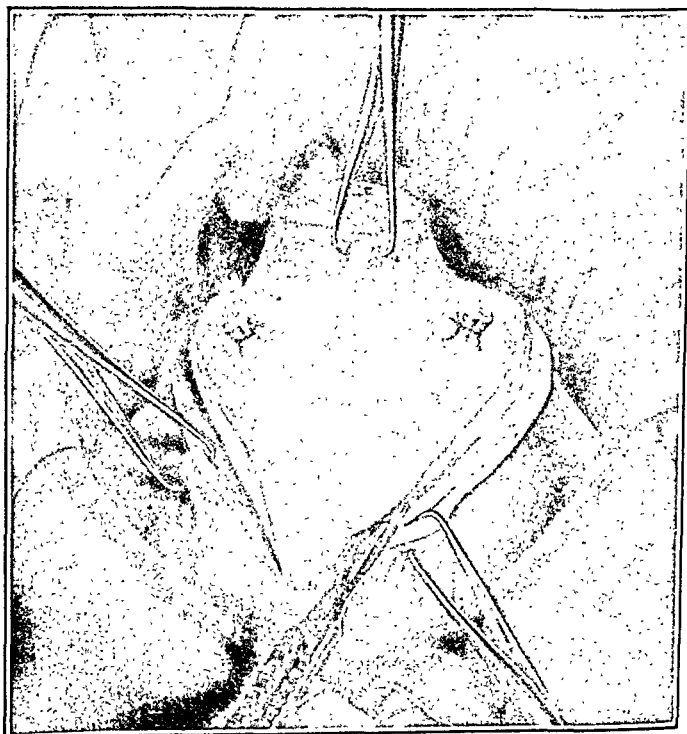


Fig. 5.—The uterus is brought through the wound and a fairly large segment is excised bloodlessly.

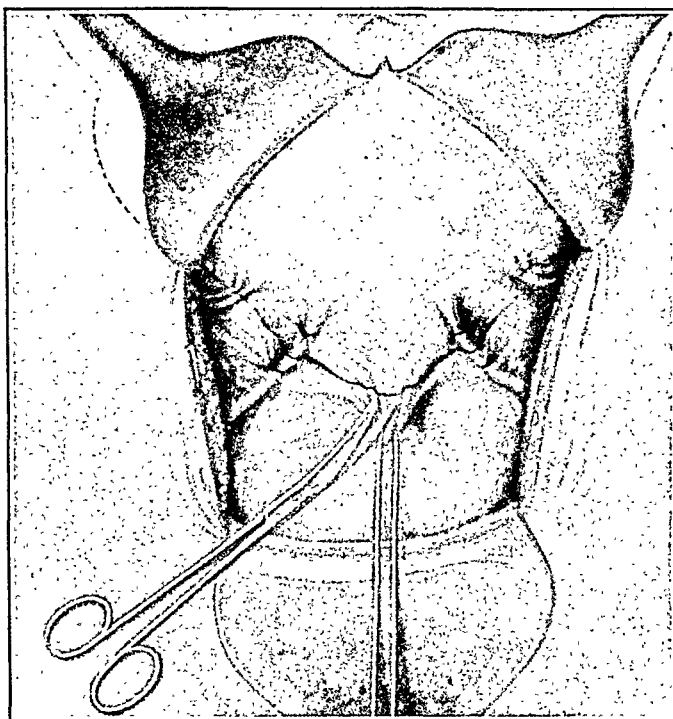


Fig. 2.—Line of incision through vesicouterine peritoneum and across round ligaments. The bulk of the myomatous uterus is in situ, preventing protrusion of intestines.

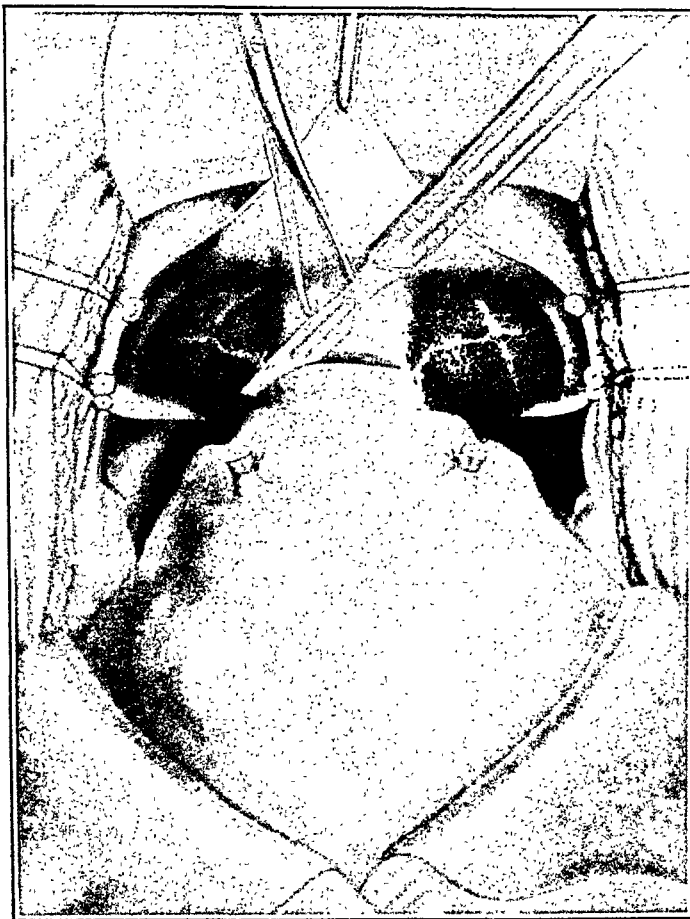


Fig. 3.—The adnexa have been ligated and severed from the uterus; the uterine vessels ligated. Cervix is cut across.

lated fundal fibroid in retrograde fashion by morecellation after ligating the pedicle and dividing it in one case, and clamping followed by division in the other. It was a simple procedure to reduce the size of the fibroid until it could be delivered easily through a relatively small abdominal incision.

The advantages of this procedure may be briefly stated:

1. The smaller incision, all other things being equal, serves to prevent large hernias.

2. As the fibromyomatous uterus is allowed to occupy its natural position during the operation, it acts as a nonirritating pad which prevents the intestines from prolapsing into the wound and from being traumatized.

3. Shock is lessened because of this circumstance and by reason of the fact that the large tumor mass is not at once delivered out of the abdominal wound.

4. Postoperative comfort appears to be comparable to that which follows the average uncomplicated vaginal hysterectomy, two principles of which are utilized in the present technic.

Over the vaginal route, it has several advantages besides the general one of thorough abdominal exploration. It affords the possibility of removing fibroids which reach as high as the xiphoid. The cervix may be retained, leaving intact the vaginal vault. Periuterine adhesions are more readily dealt with and the adnexa may be removed with greater facility, especially when they are adherent.

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Meyer, Robert, and Rockstroh, Herbert: Mucocoele and Myxoglobulosis of the Appendix and Pseudomyxoma of the Peritoneum, *Ztschr. f. Geburtsh. u. Gynäk.* 112: 125, 1936.

The authors report several of these rare conditions of the appendix. The etiology of a mucocoele presupposes a closure of the lumen with an abnormal production of mucus. Myxoglobulosis, a variety of mucocoele, results from the formation of globoid bodies from the mucus. Pseudomyxoma of the peritoneum is frequently produced by the perforation of a mucocoele or myxoglobulosis. The authors do not believe that rupture takes place directly as a result of internal pressure, but that the pressure must be augmented by an inflammatory reaction. Pseudomyxoma of the peritoneum may also be caused by the rupture of pseudomucinous cysts of the ovary. A case of pseudomyxoma of the peritoneum produced by the rupture of a mucocoele in the presence of bilateral ovarian pseudomucinous cystomas is reported as well as one case each of pseudomyxoma of the peritoneum arising from the appendix and the ovary respectively.

E. S. AUER.

above the round ligament attachments and especially at the fundus, the cervical amputation is exceedingly simple. When the fibroids are intraligamentous and fixed by adhesions, care must be taken to get into the proper plane of cleavage, avoiding bladder and ureters, a precaution important in any method of hysterectomy. This step, however, offers no greater difficulty than when the uterus is actually delivered out of the wound.

After proper disinfection, the cervix stump is sewed over and with it the round ligaments and adnexal stumps are peritonealized as in the usual technic (Fig. 4.) A pad is placed against the pelvic peritoneum. Each side of the abdominal wound is retracted by the heavy curved retractors.

The detached uterus, which has been allowed to remain in the abdomen, is now pulled through the wound by volsellum forceps and is removed piecemeal bloodlessly (Fig. 5). There need be no great hurry in doing the morcellation. The intestines are entirely out of sight. The tumor segments may be excised outside of the abdominal wound in accordance with their number, size, and distribution (Fig.



Fig. 6.—The rest of the uterus is removed in segments.

6). This proceeds until the entire uterus has been extirpated. Adhesions can be dealt with properly. The omentum, if long enough, is brought down to underlie the abdominal incision. Closure of the abdominal wound is typical.

COMMENT

The feasibility of the method will be grasped at once by the experienced pelvic surgeon. Should greater difficulty be encountered than has been anticipated, or should a malignant degeneration be suspected, it is always possible to extend the incision and then complete the hysterectomy. In one of my cases clamps were applied to the uterine vessels followed by bloodless morcellation, which made it possible to bring the much reduced uterus through the wound, after which it was amputated as in the typical hysterectomy. In two other cases I was able to remove a large peduncu-

the patients was made following the procedure adopted by Dodek and by O. W. Barlow.² A retention catheter was inserted for the duration of the period of observation.

In the initial recording period, the duration, frequency and amplitude of the contractions were ascertained. At the same time it was possible to learn from the patient, who was not in position to observe the kymograph, the onset, duration, and relative intensity of the pains. The patients described the quality of the pains in various ways such as "bad," "severe," "not bad," "mild," "crampy," etc.

The patients were used four to twenty-four hours postpartum, with the exception of one who received progestin forty-eight hours after parturition during all of which time there were severe after-pains. These subjects were comparable to the ones used in the more extensive series reported previously (Lubin and Clarke, 1936). Each was a multipara, nonmorbid, and had delivered spontaneously. Only one experienced slight hemorrhage at the time of parturition; the bleeding was controlled by pituitrin and ergotamine tartrate. Inasmuch as the effect of progestin at this early time in the puerperium on involution, red cell count, hemoglobin con-

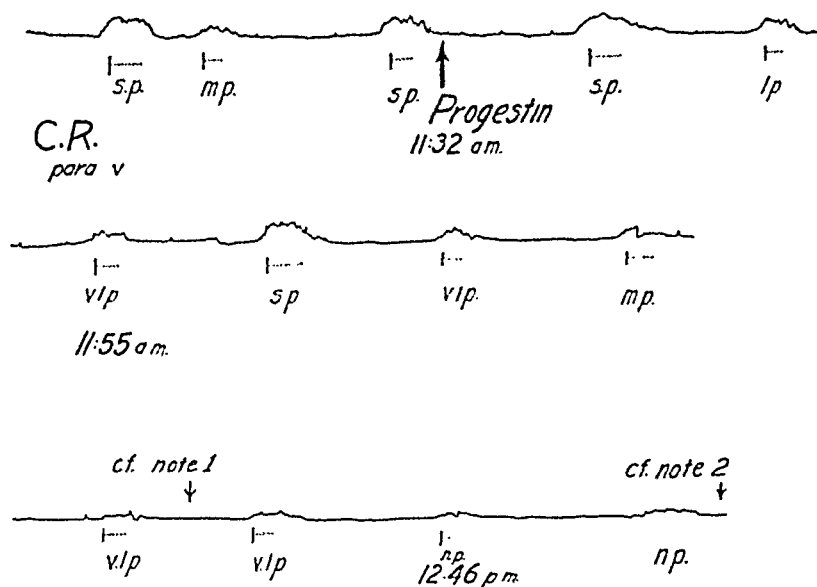


Fig. 1.—Continuous records of uterine contractions from patient C. R. (cf. Table I), aged twenty-six, para v, ten-hour labor; records taken forty-eight hours postpartum. Abbreviations are: *s.p.*, severe pain; *m.p.*, moderate pain; *l.p.*, little pain; *v.l.p.*, very little pain (nearly nil); *n.p.*, no pain.

Progestin administered at 11:32 A.M. Mild pains twenty minutes later. Onset of pain shown by vertical line under each contraction, and duration indicated by dotted line. Patient had severe pains all night, said "Pains are worse than having a baby." No return of pain in twenty-four hours.

centration and lactation was considered in the other series, these factors were not recorded at this time. Suffice it to say that the puerperal course was normal in each instance.

RESULTS

The results are briefly summarized in Tables I and II. Here it will be seen that at the outset, in each of the seven patients receiving progestin, uterine contractions of one-half to four minutes in duration oc-

²Doctor Barlow advised us in detail concerning the necessity of selecting patients with thin abdominal walls and easily palpable uteri. Furthermore, the patients must be cooperative. This latter requirement was somewhat difficult to fulfill inasmuch as the after-pains made a number of the patients unable to lie quietly for as long a time as was necessary in these experiments (one to four hours). For this reason many patients were utilized only to be discarded because of failure to complete the records.

THE RELATION OF AFTER-PAINS TO UTERINE CONTRACTIONS FOLLOWING ADMINISTRATION OF PROGESTIN

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RECENT experiments have shown that the administration of progestin to women having after-pains brings relief in most cases (89 per cent) within a few minutes to an hour (Lubin and Clarke, 1936). The present study was made to ascertain the extent to which this pain-relief is associated with abatement of uterine contractions.

It is well known clinically that after-pains are associated with intermittent uterine contractions, as stated by Williams (1930). Such painful contractions have been recorded recently during the early puerperium by Antoine (1935). It has also been observed that progestin given to women on the seventh day of the puerperium effectively inhibits uterine contractions within a few minutes (Falls, Lackner and Krohn, 1936). In this respect the inhibitory effect of progestin on the human myometrium parallels its effect upon rhythmic uterine contractility in unanesthetized rabbits (Reynolds and Allen, 1932; Allen and Reynolds, 1935) except that the onset of inhibition is more prompt in the human being.

Although after-pains are known to be associated with uterine contractions, it is equally well known that intermittent uterine contractions may occur at certain times (e.g., Braxton Hicks; puerperal, etc.) without being associated with pain. Clearly, therefore, the relief of after-pains by administration of progestin may or may not be dependent upon the abatement of uterine contractions. Determination of this point was undertaken in the present study by using the external hysterographic method of Dodek (1932) and correlating the onset and extent of pain-relief with the type of uterine contractions found after intramuscular injection of one rabbit unit (Corner-Allen unit) of progestin.

PROCEDURES

Ten patients have been studied in this investigation, seven of whom received progestin¹ after a period during which motility was recorded. The remaining three have been used for control purposes and received no progestin. Careful selection of

¹Three different commercial preparations of progestin have been used in the study of after-pains. They may be described as follows: (A) Domestic product from natural sources. This product is not crystalline material. One lot was highly active, and most used in this work (Lubin and Clarke) thus far. A second lot recently tested was only moderately effective in relieving after-pains. (B) A noncrystalline foreign product from natural sources, which failed to alter the intensity of the after-pains. (C) A crystalline domestic preparation. Used only to a slight extent thus far, but highly effective in the relief of after-pains.

TABLE I
OCCURRENCE OF AFTER-PAINS AND UTERINE CONTRACTIONS IN WOMEN WITH PROGESTIN THERAPY

PATIENT	PAIN		UTERINE MOTILITY		END-RESULTS		REMARKS
	BEFORE PROGESTIN	AFTER PROGESTIN	BEFORE PROGESTIN	AFTER PROGESTIN	PAIN	MOTILITY	
S. G.	Severe	Less severe in 15 min.; very mild in 1 hour	1 min. duration. 4 min. intervals	1 hr. later, very weak contractions with each mild pain. Duration same, and frequency increased	Relieved	Decreased	Para iii, 7 hr. labor, spontaneous delivery. Slight hemorrhage at labor, controlled by pituitrin and gynecen. 4 hours postpartum
I. M.	Severe	Less severe in 25 min. and continued mild	2 min. duration. 15 min. intervals	No change	Relieved	No change	Para ii, 9 hr. labor, spontaneous delivery. 48 hr. postpartum
N. N.	Severe	Less severe in 6 min.; mild in 45 min.	2 min. duration. 6 min. intervals	No change	Relieved	No change	Multipara, 12 hr. labor, spontaneous delivery 24 hr. postpartum
R. P.	Moderate	Less severe in 45 min.; mild in 1 hr.	2-3 min. duration. 5 min. intervals	1 hr. later, reduced amplitude; duration and frequency same	Relieved	Decreased	Para ii, spontaneous delivery. Severe pains all day before. 24 hr. postpartum

curred at intervals of from four to twenty minutes. The pains occurred during part of these contractions, as noted below.

Pain-Relief.—Relief from the after-pains was obtained in each instance after the use of progestin. As a rule, the pains were noticeably milder within fifteen minutes or less, and were reported to be very mild or absent within one-half to one hour following the injection. As noted in the earlier larger series, the pain-relief persisted with only occasional recurrence at the time of nursing in some instances.

Uterine Contractions After Progestin.—In none of the seven patients receiving progestin did motility cease within the time of recording. It did become distinctly less in three patients, however, and slightly less in one. This change affected the amplitude (height) of the recorded contractions, and in one instance (S. G.), the frequency also. The reduction in amplitude was relative to the amplitude of the pre-injection motility. It may be noted also that the external hysterographic technic does not record all phases of the uterine contractions but only those which are localized under the plunger of the recording apparatus. Nevertheless, the duration and

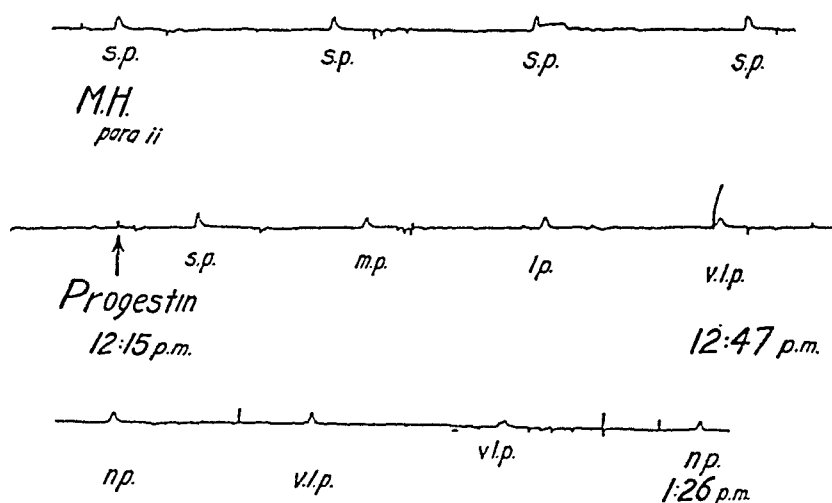


Fig. 2.—Patient M. H. (cf. Table I). Para ii, thirty-eight hour labor, spontaneous delivery, eighteen hours postpartum. Abbreviations as in Fig. 1.

Progestin given at 12:15 p.m. Mild pains in twenty minutes, nil in thirty-five minutes. Had after-pains all night and morning. Pain relieved when contractions persisted, with only slight decrease in amplitude. Pains began after contraction started and outlasted the period of relaxation (cf. text). At 12:47 patient coughed, giving large deflection of writing point.

frequency of the contractions were not significantly altered in any case receiving progestin, and in two of the three uninjected patients the contractions diminished spontaneously.

The time of onset of the reduced amplitude of contractions deserves special comment; it did not become significantly less within three-fourths of an hour in any instance. Thus the pain-relief preceded recognizable changes in the height of contractions. In four of the patients, moreover, there was pain-relief but no significant change in the type of the contractions observed. *Clearly, therefore, relief of after-pains following the use of progestin is not necessarily associated with striking changes in motility, as gauged by this method of recording uterine contractions.*

Falls, Lackner, and Krohn (1936) find with the intrauterine balloon method of recording that one will obtain cessation of uterine contractions following progestin on the seventh day of the puerperium. This inhibition takes place within a short time after the administration of even smaller amounts of progestin (1 Clauberg unit) than were used in our experiments. Perhaps some difference in sensitivity

of the uterus at that time (seventh day of the puerperium) or some difference inherent in the two methods of recording may account for the variations in intensity and onset of inhibition recorded by the two methods respectively.

Occurrence of After-Pains in Relation to Uterine Contractions.—The relationship between the time of onset of the after-pains and of onset of the contractions was frequently noted. It was found that pain became evident as the contraction approached its peak. A similar situation is frequently encountered during labor, at which time uterine contractions may be palpated before the associated pains are experienced by the patient. In some instances the pain persisted through the highest portion of the contraction, whereas in others it continued well into the relaxation phase of the contraction.

TABLE II
SUMMARY OF DATA OF TABLE I

PAIN		UTERINE CONTRACTIONS	
Relieved	7	Diminished	3
Unrelieved	0	Slightly diminished	1
		No change	3

DISCUSSION

The present results confirm the earlier ones in showing that after-pains may be relieved by suitable administration of progesterin. This pain, however, is relieved before significant diminution of motility takes place, as revealed by the external hysterographic method. A question naturally arises, therefore, concerning the mechanism by which the pain is brought about. By what functional change is pain-relief achieved, since contractions of considerable force occur when the pains commence to subside?

In this connection reference may be made to the experiments of Moir (1934). This investigator found that in a young woman having intense menstrual pain, the onset of pain was coincident, not with the beginning of the contraction, but with the occurrence of an intrauterine pressure which exceeded the level of systolic blood pressure, taken simultaneously in the brachial artery. Because of this fact, he suggests that the pain may arise as a result of prolonged ischemia of the uterus during the contraction phase of its activity. Painter and Harne (1936) find a somewhat similar situation in the case of sensory disturbances resulting from experimental alteration of intrauterine pressure in the rat.

In view of these considerations, as well as our own observation on the time of onset of pain, it seems reasonable to explain the results of the present study on the grounds that ischemia of the uterus occurs during the contraction phase to such an extent that pain results, and that progesterin in some way relieves the extent of the ischemic condition in the myometrium. Our data do not prove this although they do provide a basis upon which relief of uterine pain by means of progesterin may be tentatively explained.

TABLE I—CONT'D.

C. R.	Severe	Mild in 20 min. Nil in 1 hr. Grateful for relief	2-3 min. duration. 10 min. intervals	Weak 1 hr. later, frequency unaffected	Relieved	Decreased	Para v, 10 hr. labor, spontaneous delivery. Had severe pains all night. 24 hr. postpartum
M. S.	Moderate	Less severe in 8 min.; very mild in 1 hr.	2 min. duration. 5 min. intervals	No change	Relieved	No change	Para ii, 3 hr. labor. 15 hr. postpartum
M. H.	Severe	Less severe in 15 min.; very mild in 35 min.	1½ min. duration. 15 min. intervals	Slight weak	Relieved	Slight decrease	Para iii, 38 hr. labor; pain all night and morning. 18 hr. postpartum
Controls E. N.	No real pain. Felt each contraction		1 min. duration. 5 min. intervals				Para iii, 4½ hr. labor, spontaneous delivery, contractions decreased spontaneously, waiting to use progestin
G. F.	Cramplike		2 min. duration. 10 min. intervals				Para iii, 17 hr. labor, spontaneous delivery. Nervous; weak; contractions decreased spontaneously, waiting to use progestin
M. M.	Mild		4 min. duration. 15 min. intervals				Para i, 6½ hr. labor, spontaneous delivery premature. Contractions did not disappear; no progestin used

We make this assertion, first, because our results are good, and second, because the length of hospitalization is considerably less than is ordinarily estimated for patients treated conservatively.

METHOD

Our routine is as follows: The general physical and pelvic examinations, together with laboratory findings, are used to determine the condition of the patient. Especial note is made of the amount of bleeding, amount of dilatation of the cervix, size of the fundus, and degree of tenderness of the parametrium and peritoneum. If placental tissue is protruding from the cervical os, it is removed with aseptic precautions. If there is little or no bleeding and the fundus is only slightly enlarged, or if there is a history of expulsion of the products of gestation, the patient is put under observation and treated expectantly. Patients who bleed moderately or severely are treated surgically without delay unless marked tenderness of the parametrium or moderate tenderness of the peritoneum is present. Either is always considered a contraindication to surgery. As a rule, the temperature is disregarded, but if fever is accompanied by a pulse rate of over 120, the possibility of a blood stream infection must be considered, and surgical treatment is postponed until the absence of septicemia has been determined.

Our surgical procedure consists of *dilatation and evacuation*. We wish to emphasize the fact that we do *not* curette. After the cervix has been carefully dilated sufficiently to admit a sponge forceps, 1 c.c. of obstetric pituitrin is given intramuscularly. As soon as contraction of the fundus has taken place, permitting the uterine cavity to be easily outlined, a sponge forceps or a placental forceps is used to remove the products of gestation. This is done very gently because of the danger of perforation, even with the use of such blunt instruments. After the uterine cavity is grossly empty a fairly large, blunt curette is used to *sound* the cavity for any large pieces of placenta which may have been left. If such are found, we again employ the sponge forceps for their removal, but we *do not* curette. A gauze pack soaked in a solution of alcohol, glycerin, and formalin* is gently inserted into the uterine cavity and allowed to remain for twenty-four hours. This is an effective means of removing any small adherent placental remnants, and at the same time it hastens coagulation of the surface of the uterine cavity. Occasionally an alarming hemorrhage occurs as soon as the operative procedure is begun, in which event all attempts at evacuation are immediately discontinued, and the uterus is tightly packed. After twenty-four hours, evacuation usually can be accomplished without further difficulty.

RESULTS

In the five-year period covered by this report (March, 1930 to March, 1935), 730 patients with incomplete abortions were admitted to the Stanford Gynecologic Service of the San Francisco Hospital. Of these, 605 were treated by *dilatation and evacuation*, with an average hospital stay of 6.02 days per patient. Three of these patients reentered the hospital because of recurrent bleeding, and were again treated surgically. The remaining 125 were treated conservatively, either because of little or no bleeding or because of infection extending beyond the uterus. For this group, the average hospital stay was 14.4 days per patient. Seventeen of the patients who received conservative therapy returned because of recurrent bleeding, and *dilatation and evacuation* was performed.

Infection was present clinically in approximately 85 per cent of all cases, as evidenced by fever and leucocytosis. Microscopically, 72 per cent of the placental tissue showed infection (Table I).

*Alcohol 95 per cent 10 ounces, glycerin 6 ounces, formalin 10 per cent 10 drops.

CONCLUSIONS

1. After-pains may be relieved by intramuscular injection of 1 rabbit unit (Corner-Allen) of progestin.
2. Pain-relief begins prior to any significant alteration in uterine contractions; as revealed by the external hysterographic method of recording.
3. The mechanism by which after-pains are produced is considered and the nature of the relief from them following progestin therapy is discussed.
4. It is tentatively concluded that the relief of uterine pain following injection of progestin is associated with prevention (completely or relatively) of an ischemic condition within the uterus during a portion of its contraction phase.

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A FIVE-YEAR STUDY OF INCOMPLETE ABORTIONS AT THE SAN FRANCISCO HOSPITAL

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A LARGE proportion of the patients admitted to the Stanford Gynecologic Service at the San Francisco Hospital suffer from the effects of incomplete abortion. The majority of these abortions are self-induced, and consequently are usually accompanied by infections of varying severity. There always have been two opposed modes of treatment of this extremely common condition, viz., the conservative and the radical. Since there still exist considerable confusion and divergence of opinion as to what constitutes the most efficacious and least dangerous method of treatment, we believe that a report of the results of our mode of therapy may be of interest. The method followed by us was adopted some twenty years ago, and differs in some respects from the generally accepted orthodox principles laid down for the treatment of abortion. The results published here cover the last five years.

Although our method of treatment must be classed as radical, we believe it to be as safe, or safer than the ultraconservative procedures.

5. A. R., aged twenty-five years. Entered and refused treatment. Reentered four days later with profuse bleeding. On entry, temperature 103°, pulse 130, and respiration 30. Fundus large and boggy, with much induration in the parametrium. *Dilatation and evacuation* performed, with transfusion, which was repeated twenty-four hours later. Died five days after entry. Coroner's autopsy showed septic abortion.

DISCUSSION

On the basis of the results reported here, we feel that our method of treating incomplete abortion is both satisfactory and safe. However, may we emphasize again that we do not advocate radical curettage, but follow a middle course by evacuating the uterus with as little trauma as possible. We are convinced that emptying the uterus of infected material by the above-described technic decreases the chance of extension of infection to the parametrium and peritoneum, lessens the likelihood of a septicemia, shortens the period of hospitalization, reduces blood loss, and expedites recovery.

TABLE II

AUTHOR	NO. CASES	TYPE OF TREATMENT	MORTALITY
Reichelt, H.	1870	Conservative and radical	2.02%
Sommer, K., and Ziegeler, H.	1150	Conservative	2.00%
Olow, J.	740	Radical	0.40%
Harbitz, H.	3791	Conservative and radical	2.16%
Watkins, R.	341	Conservative	0.88%
Balslev, L.	1600	Conservative	7.08%
Schroeder, R., and Clauberg, C.	473	Conservative	1.00%
Hillis, D.	1000	Radical	2.00%
Winter, H.	6512	Radical	3.08%
Tuttle, H.	1164	Radical	2.23%

Table II gives the mortality figures of the largest series of cases reported in the last ten years. It is evident that there is no appreciable difference in the number of deaths reported for conservative and for radical treatment. Our mortality of 0.68 per cent compares very favorably with the lowest figures reported. Other factors, such as periods of morbidity, hospital days, and after-effects, are not easily compared with reports of other observers because of lack of figures in certain publications.

Miller and Bubis advocate conservative treatment, but give no statistics. Gellhorn and Harbitz suggest a compromise between the conservative and the radical methods, while Schulze, Olow, and Wahl make a plea for the radical procedure. Watkins is of the opinion that conservative treatment is the procedure of choice, contending that curettage favors the spread of the infection to the parametrium, thus lengthening the period of convalescence. It is interesting that he stresses the rapid decline in temperature following spontaneous expulsion of the uterine contents, a result which also has been very evident in our method of treatment. Schulze, on the same basis, favors radical treatment. He contends that emptying the uterus of its foreign and infected material stimulates it to contract and controls bleeding, and thus conserves the patient's energy, giving her a chance for a more rapid recovery.

Pelvic abscesses occurred in three patients, and were treated by drainage through posterior colpotomy incisions. One of these patients died, probably from exsanguination rather than from sepsis. The other two had uneventful immediate recoveries from drainage of the abscesses, but subsequently were operated upon for low-grade pelvic inflammatory disease which undoubtedly resulted from the infected abortions.

Vaginal hysterotomy was performed on one patient approximately four months pregnant, because of excessive bleeding and resistance of the cervix to mechanical dilatation. We consider hysterotomy a valuable procedure when pregnancy has advanced to the second trimester if the cervix is very long and will not yield to dilatation. Accidents of pregnancy of more than sixteen weeks are not included in this report.

TABLE I

Number of incomplete abortions	730
Treated by dilatation and evacuation	605
Average stay in the hospital	6.02 days
Treated conservatively	125
Average stay in the hospital	14.4 days
Reentries after dilatation and evacuation	3
Reentries after conservative treatment	17
Infected cases	525 (or 72%)
Gross mortality	5 (or 0.68%)
Corrected mortality	3 (or 0.41%)

A hemoglobin of 50 per cent or less, determined by the Sahli standard, was considered a definite indication for blood transfusion, although we were not always able to obtain donors for these indigent patients. Whenever possible, transfusion should be given in order to raise the general resistance to infection.

There were five deaths in this series of 730 patients, constituting a mortality of 0.68 per cent. This figure may be corrected to 0.41 per cent, since two of these patients were admitted in extremis and died before adequate treatment could be instituted. The other three presented pictures of general septicemia on admittance, and as a result died within eight days.

SUMMARY OF MORTALITY GROUP

1. A. H., aged thirty-six years, three months pregnant. No history of abortion admitted. On entry, temperature 99.8°, pulse 138, and respiration 30. *Dilatation and evacuation* performed because of profuse bleeding. Died six hours after entry. Coroner's autopsy showed pelvic abscess with old perforation of uterus, incomplete abortion.

2. E. L., aged twenty-nine years, four months pregnant. Used slippery elm four days prior to entry. On entry, temperature 100°, pulse 90, and respiration 24. Abdomen moderately tense. Uterus and adnexa tender. Given general supportive measures. Died forty hours after entry. Coroner's autopsy showed peritonitis and septicemia following abortion.

3. G. C., aged thirty-six years. No history obtained. On entry, temperature 102°, hemoglobin indeterminable. *Dilatation and evacuation* performed, with transfusion of 750 c.c. whole blood. Died six hours after entry. Coroner's autopsy showed incomplete abortion, sepsis, exsanguination.

4. A. H., aged twenty-seven years. Did not admit abortion. History of bleeding for two weeks after three months amenorrhea. On entry, temperature 102°, pulse 134, and respiration 36. Vomiting, abdomen tense, chest clear, no severe bleeding. Given general supportive measures. Gradual downhill course with high temperature and pulse. Died eight days after entry. Coroner's autopsy showed peritonitis and endometritis, bilateral salpingitis and oophoritis.

REACTIONS OF HUMAN UTERINE MUSCLE IN VITRO TO PITUITRIN, ADRENALIN AND ACETYLCHOLINE AND THEIR RELATIONS TO THE MENSTRUAL CYCLE

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MUSCLE strips, approximately 10 by 3 by 3 mm., from human uteri obtained at operation in Sloane Hospital, were examined. These were suspended, by the usual technic for kymograph recording, in 100 c.c. of Ringer's solution at 37.5° C. The lever weight and the magnification on the kymograph record were constant. The spontaneous rhythms of about 350 of these strips and their responses to the addition to the Ringer's solution of pituitrin (0.5 c.c., 5 units) were recorded. More than five hundred strips were also studied with adrenalin (0.1 c.c. of a 1:1,000 solution) and acetyl choline (50 mg. of the hydrobromide). The clinical history and examination of the endometrium, and frequently of the ovary, indicated for each case the time in the menstrual cycle at which the specimen was obtained. All days of the cycle were represented except the second to the fifth (as a rule, operations are not performed during menstruation). With a few exceptions which will be noted later, only uteri within the childbearing age were used. No uteri with demonstrable pathologic conditions were used, with the exception of some in which one or two small fibroids occurred.

If the strips showed no spontaneous rhythmic contraction within an hour after they were set up in the recording apparatus, they were discarded. Such lack of motility may possibly be due to differences in the conditions of the hysterectomy (the anesthesia was gas-oxygen and ether in almost all cases). It definitely did not correlate with the time in the menstrual cycle, nor the time elapsed since the operation.

Strips from different uteri, set up in parallel in the same suspension cylinder, exhibited their different rhythms independently. Parallel strips from the same uterus usually showed the same rhythm. It was repeatedly noted that a strip contracting rhythmically and untreated may abruptly and spontaneously alter its rhythm, both as to timing and magnitude of excursion. Such changes may occur several times with one strip, and at any period during the time that it retains its activity. These observations throw doubt on the suggestions which have been made concerning the correlation of type of contraction-rhythm with the time of the menstrual cycle; we have found no indication of such a rela-

Witherspoon reports 200 cases with 7 deaths due to perforation of the uterus, an accident which is negligible in our series, and, we believe, avoidable, provided all points described in our technic are rigidly observed. In our study of 730 abortions, only one death occurred from perforation, and this was probably the result of the patient's own attempt at abortion, since the autopsy showed an *old* perforation.

Whether our procedure is followed by a low-grade parametritis after the patients leave our care is difficult to ascertain. It seems to us that infected, necrotic placental tissue, if allowed to remain in the uterus for any length of time, is more likely to invite parametritis than if gently removed with the least possible traumatization of tissues. Since very few of our patients have been readmitted to the hospital service or have attended the clinics for prolonged after-treatment, we have concluded that our incidence of extrauterine infection is low.

CONCLUSIONS

1. A middle course between conservative and radical measures is advocated for the treatment of incomplete abortion, as exemplified by *dilatation and evacuation*.

2. A comparative study of 730 patients, 605 of whom were treated surgically and 125 expectantly, shows that such a procedure is both safe and expedient.

3. The method of treatment described shortens the period of hospitalization.

4. The mortality rate following this procedure is comparatively low.

5. Extension of infection beyond the uterus or the presence of septicemia is a contraindication to *dilatation and evacuation*. Such cases should be treated expectantly.

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were rather enhanced in magnitude. This case seems to be of interest in view of the observations of Novak on evidence of "genital rejuvenation" with granulosa cell tumors of the ovary.

Robson has reported interesting studies on the relation of estrin to uterine reactivity. In vitro tests with the human muscle addition of amniotin (probably a mixture of estrogenic substances) to the suspension fluid gave no marked effects, although the tone of the strip seemed to be stabilized; in some cases a diminution of the speed and amplitude of the rhythm appeared, while in other cases, in which the rhythm was unaffected or increased, the intensity of response to the drugs appeared to be somewhat enhanced.

These observations illustrate the frequent variability of reaction of uterine muscle to a given drug dose. They are consistent with the view that the response may be conditioned by the hormonal balance of the tissue, but they cannot be reconciled to the hormonal and menstrual cycle relations as claimed by Knaus. They also, when compared with the recorded results on rabbit and other uteri, add emphasis to the difficulty of transferring conclusions obtained from data on other species to the physiology and pharmacology of the human uterus. We believe also that the data on adrenalin and acetyl choline must be interpreted simply as relating to the action of these as drugs on the cell rather than necessarily implying the intervention of nerve end-structures of sympathetic or parasympathetic type.

We are indebted to Professor Benjamin P. Watson for constant encouragement and advice, and for his placing the large material of the Sloane Hospital for Women and the Vanderbilt Clinic at our disposal. We also wish to thank Professor Charles C. Lieb and Professor Michael G. Mulinos of the Department of Pharmacology for their kind advice and assistance in both the technic and the interpretation of these results.

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The following suggestions are made to prevent the transmission of syphilis by blood transfusion and to secure for the patient a maximum of safety. The procedure of blood transfusion should be carried out by competent and well-trained men. Institutional work should be guided by a physician who is qualified and who should insist upon a minute examination of blood donors at frequent intervals for the presence of a syphilitic infection. There should be available at all times the facilities of a laboratory wherein the common serologic examinations of donor's and recipient's blood for the presence of a syphilitic infection is conducted. The examination should be made on the day of transfusion. The laboratory reports should be written, and not telephoned. Such reports should be made by a competent technician. All syphilitics are potential transmitters.

C. O. MALAND.

tion. Also, in repeated comparisons with strips taken from different layers or in different planes from the same uterus, we found no consistent differences. We could not relate the occurrence of these variations with the menstrual cycle nor with any other observable variable.

Approximately 90 per cent of the uterine strips contracted when treated with pituitrin. This response occurred throughout the cycle; it was noted, however, that from about the twentieth day on there was an increase in the magnitude of the response. On 10 per cent of the strips pituitrin had no effect; there was no correlation between this lack of response and the time in the cycle, such cases being found at any period. In one case only (on the eleventh day of the cycle) pituitrin caused relaxation. These results appear to contradict the conclusions of Knaus concerning the close relationship between corpus luteum function and the time in the cycle and the reactivity of the uterine muscle to pituitrin.

It was observed that repeated washing of a muscle with Ringer's solution might alter its reactivity. Such treatment in some cases activated an inactive uterus; in other instances it abolished, and in others increased, the subsequent response to pituitrin.

Adrenalin contracted 88 per cent, had no effect on 2 per cent, and relaxed 10 per cent, again without any correlation between the time in the menstrual cycle and the occurrence of atypical responses. Acetylcholine caused contraction in all cases, but with considerable variability in intensity of response. With both of these drugs it was observed that the magnitude of response tended to increase from about the twentieth day on, although this was not as marked as in the case of pituitrin.

Twelve strips which were treated with atropine (in amount not in itself causing any alteration of the normal rhythm) responded to subsequent adrenalin treatment by relaxation.

Addition of ergosterol to the Ringer's solution, in 9 of 12 cases so treated, abolished the response to subsequent acetylcholine treatment. This is in accord with the observations of Carter and Mapson on the interaction between sterols and acetylcholine in frog gastrocnemius and heart muscle. In 3 cases the ergosterol caused a reversal of the response; thorough washing with Ringer's solution abolished this reversal.

Strips from 6 postmenopause uteri were tested. Their tone was unstable, their rhythmic contraction feeble or lacking, and their responses to the drugs were slight or absent. A seventh case gave different results. This was a uterus from a woman sixty-three years old, fifteen years postmenopause. The pathologist's report indicated a cystadenoma of the ovary; there were numerous metastatic growths throughout the pelvis and abdomen. The muscle showed rhythmic activity and the drug responses, which were of the type normal for premenopause uteri,

An x-ray of the chest on April 13, 1935, showed lobar pneumonia and cardiac enlargement. The electrocardiogram on April 16 (Fig. 1) showed second degree heart-block with an auriculoventricular conduction time of 0.32 second. The auricular rate was about 100 and the ventricular about 50 per minute. Aside from this and from a tendency toward left axis deviation, there were no other significant changes.

The patient showed a rapid progressive improvement. The temperature became normal the seventh day after admission and remained so until discharge. The pulse ranged between 84 and 40 per minute.

Fig. 1.

Fig. 2.

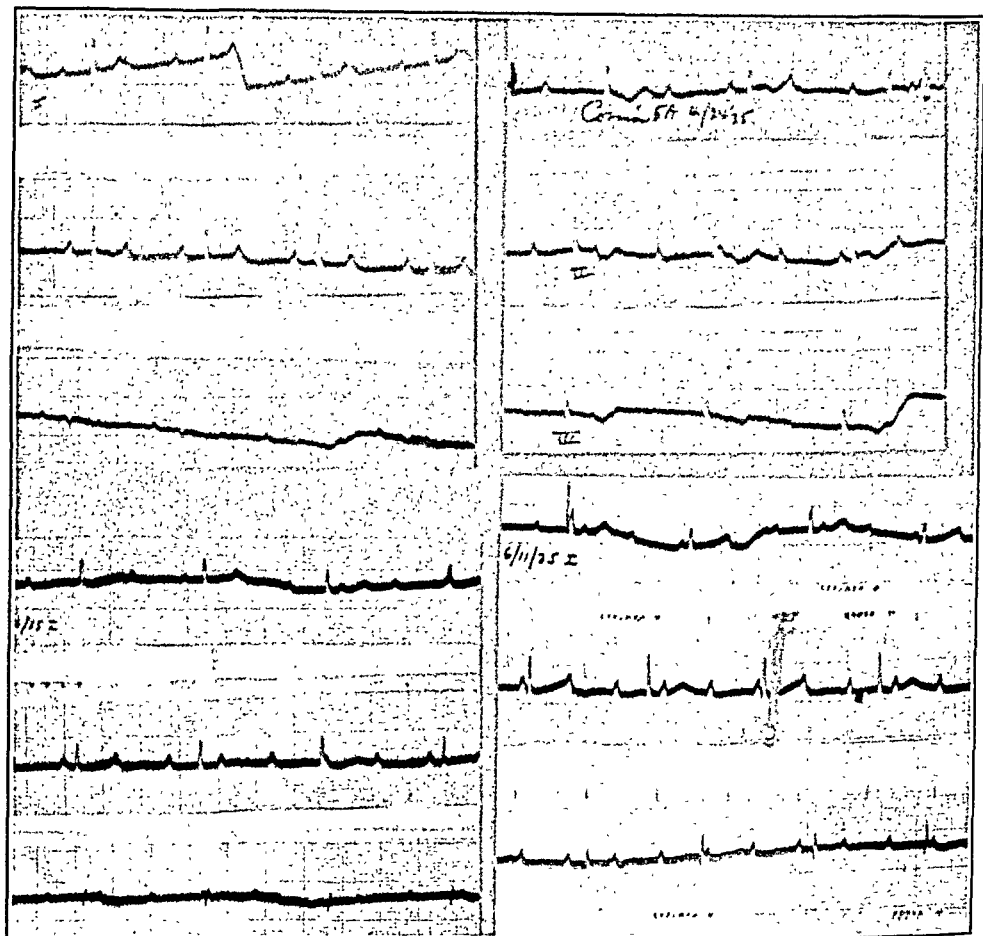


Fig. 3.

Fig. 4.

On April 22, the heart appeared to approach the normal in size. The systolic murmur and accentuated first sound were still present. The ventricular rate was about 42 and a faint short sound was heard at the left costosternal junction on and off, in addition to the regular heart sounds, presumably due to auricular contractions. Complete auriculoventricular block was the diagnosis.

It was felt at this time, in view of the absence of a definite history of rheumatism and the questionable reliance on the patient's history of preexisting heart disease, that the heart-block was caused by pneumonia. This opinion was fortified by another electrocardiogram taken on April 24, 1935 (Fig. 2), which showed complete instead of partial auriculoventricular block. In addition, there were changes in the configuration of the ventricular complexes, indicating alterations in the myocardial state. Such changes were negative T-waves in all leads, and diminu-

HEART-BLOCK AND PNEUMONIA COMPLICATING PREGNANCY

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COMPARATIVELY few cases of heart-block complicating pregnancy were reported in the literature. Greenhill's review¹ up to 1933 shows only 12 reported cases, including his one case. Since then one more case was reported by Bernstein,² making a total of 13 cases.

The main reason for this comparative sparsity of case reports is that complete heart-block in itself is an uncommon condition and is more so before the age of forty and in females. The frequency of pneumonia occurring during pregnancy likewise is very small, judging from the reported cases, and the fatality from it is rather high.

I found no references in the literature of the coexistence of heart-block and pneumonia as complications of pregnancy. The following case showing this condition is therefore of interest.

G. C., white, twenty-seven years old, admitted to the Obstetrical Division of the Coney Island Hospital on April 12, 1935, with complaints of cough and bloody expectoration, pain on both sides of the chest on breathing and dyspnea of four days' duration. There was amenorrhea for the past six months with definite signs of pregnancy. The family history was essentially negative. In her past personal history, she mentioned that she was subject to frequent colds, was told that she had heart trouble about two years previously, and that she was pregnant a year before this present pregnancy, at which time she aborted at four months.

The onset of the present illness dated back one week prior to admission, when she contracted a "cold." The nose and eyes were running and there was a dry cough, which later became productive and blood-tinged. This was associated with sharp pain in the chest, more so on the right and more pronounced on deep breathing and coughing. Four days prior to admission, she developed a severe chill which lasted a few minutes.

The physical examination showed her to be in apparent distress. There were marked dyspnea, moderate cyanosis of the lips and dilatation of the alae nasae. Her mentality was clear and she was cooperative. Her temperature was 104.2°, pulse 80, and respiration 60. The blood pressure was 124 systolic and 48 diastolic. Her dental hygiene was poor. The tongue was coated and the pharynx was injected. The lungs showed dullness merging with flatness and diminished breath sounds at the right base. The upper portion of the right base showed bronchial breathing and many fine medium inspiratory rales. There were also dullness and diminished breath sounds over the left lower lobe. The heart was enlarged both to the right and to the left. The sounds were accentuated, P_2 being greater than A_2 . There was a systolic murmur heard along the left sternal border with greatest intensity over the mitral area. The uterus extended about $2\frac{1}{2}$ fingers above the umbilicus. Fetal heart sounds were heard at the right lower quadrant, with a rate of 190 and regular. It was difficult to map out the fetal parts. The extremities showed no abnormalities.

The diagnosis was: (1) Lobar pneumonia; (2) seventh month pregnancy, and (3) old rheumatic heart disease in the form of mitral insufficiency.

treat heart-block or any other cardiac case at the mere presence of the condition, which is erroneous. In the absence of symptoms of cardiac insufficiency or of the anginal syndrome, no treatment is necessary regardless of what the cardiac condition might be. In the presence of symptoms, however, proper therapy must be used.

The most common manifestations of the terminal stages in complete heart-block are congestive failure, the anginal syndrome or the Stokes-Adams syndrome. The first requires rest in bed and diuresis. The second may require antispasmodics, sedatives, narcotics, or other medication. The third may respond to adrenalin. Digitalis should not be used in cases of partial heart-block with congestive failure, but it may be used in exceptional cases of complete heart-block with congestive failure, where all traces of vagal influence are gone. Even here it must be used with great caution, and under careful supervision, and its value is questionable.

In my discussion of the prognosis of heart-block, I have, of course, not included the cases of arteriosclerotic origin. These usually have a poor prognosis, but do not enter into our discussion here. We are dealing with block earlier in life before the arteriosclerotic age. It must be realized, however, that even in earlier life the prognosis of the condition is grave where the myocardium is greatly damaged, or where the etiologic factor is continuously operative and is irremovable.

SUMMARY

A case of complete heart-block and pneumonia complicating pregnancy with a successful termination is reported. On the review of the literature no similar case was found, and only 13 cases of complete heart-block alone in pregnancy were reported to date, exclusive of this case. The favorable prognosis and the importance of withholding any therapy in asymptomatic heart-block or any other form of compensated heart disease during pregnancy is stressed.

I am indebted to Dr. Harvey B. Matthews, Director, and Drs. Paul E. Wesenberg and Maurice G. Derbrücke, Attendants, Department of Obstetrics, Coney Island Hospital, for the privilege of observing this case from their department.

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Moran, Clarence S.: Fibro-Adenoma of the Breast During Pregnancy and Lactation, Arch. Surg. 31: 688, 1935.

The writer reports on 27 fibroadenomas of the breast removed during pregnancy and lactation. It was observed that the tumors under these conditions were modified, the changes being similar to those in the surrounding normal breast.

Any lump noted in the breast during pregnancy and lactation should be explored immediately unless the patient is under twenty-five or unless the lesion resembles a mastitis. In the latter case two weeks may be allowed for involution or abscess formation. The patient should be prepared for radical operation when removal of tissue for biopsy is undertaken. It is preferable to remove the tumor during pregnancy when the breast is less vascular. If the tumor is larger than one quadrant of the breast and is of the spindle cell type, it should be treated as a sarcoma.

HUGO EHRENFEST.

tion in the tendency toward left axis deviation. This was substantiated by another electrocardiogram done on April 26, 1935, which is not reproduced here and which showed again complete heart-block and further changes in the T-waves. The mitral insufficiency could be explained on the basis of dilatation of the auriculoventricular ring.

The patient was discharged from the hospital improved on April 27, 1935, and was followed in the cardiac clinic. During this time she showed little diminution in her cardiac functional state, although complete heart-block was still present. An electrocardiogram taken in the clinic on May 16, 1935 (Fig. 3), still showed complete heart-block, but there was a slight change of the electrical axis toward the left, and the previously negative T-wave assumed a positive phase in all leads, with a diphasic tendency in the third lead.

The patient was readmitted on June 10, 1935. Her general condition was excellent. A tracing taken one day after the second admission (Fig. 4) showed the T-wave in all leads to be more markedly positive and the electrical axis was within normal limits, indicating further changes and improvement in the myocardial condition. Complete heart-block was still present, however. She was delivered of a normal child on June 12, 1935. The placenta had to be removed manually. She ran a normal postpartum course and was discharged on June 20, 1935.

DISCUSSION

We recognize three degrees of heart-block. The first degree is that in which there is a mere prolongation in the time necessary for the spread of the electrical impulse in the heart; the second, where there is an occasional interruption of the impulse; and the third, where there is a complete interruption of all impulses coming down from the auricles to the ventricles. The last results in complete auriculoventricular dissociation or complete heart-block. The first and second degrees are by far more frequent and less serious than the third degree. The case presented here started as a second degree block and developed later into complete block.

The most common cause of heart-block is degeneration of the heart associated with arteriosclerosis. For this reason, the prevalence of heart-block is much greater after forty years of age. Other causes are various infectious diseases such as rheumatic fever, influenza, pneumonia, diphtheria, syphilis and so on; congenital defects in the conduction apparatus; various intoxications, especially that of digitalis and quinidine; anoxemia, and vagal stimulation. The last may be demonstrated by carotid sinus pressure, which in susceptible individuals may result in reflex vagal block, as I previously described.³ In our case the condition evidently resulted from the pneumonia, for it started as a partial block and ended in complete block. Besides other progressive changes were noted in the myocardial state in the course of the disease.

The prognosis of heart-block does not depend merely upon its existence but upon the operative causes and associated myocardial disease. Where the etiologic factor is entirely removed and the heart muscle is left in good condition, the prognosis is good. This is true in our case. There are many cases on record where individuals with complete heart-block lived in comparative comfort for many years. Among the reported cases of heart-block in pregnancy, there were Hermann and King's case,⁴ who had 6 successful deliveries without complications; Freund's case⁴ with 7 normal deliveries; McIlroy and Randall's patient,⁴ who went through two gestations, the second of which was a delivery of twins. The interesting factors in our case are that the patient recovered from the pneumonia in spite of the coexisting heart-block, and the pregnancy was not interfered with in any way, the delivery having been uneventful and the condition of the fetus unaffected.

The treatment in this case consisted merely of bed rest and general care during the pneumonic period. This is stressed because we are always likely to attempt to

R.B.C., 8,800 W.B.C., 69 per cent polynuclears, 26 per cent lymphocytes, 2 monocytes, and 3 eosinophiles. Color index, 0.77. Sedimentation time, took twenty-five minutes for the level to fall to 24 mm.

On the fifth day the patient was taken to the operating room and a laparotomy performed. Convalescence was entirely uneventful and the patient was discharged on the fifteenth postoperative day.

Macroscopic examination of part of both fallopian tubes and left ovary showed that one tube was 2 by $1\frac{1}{2}$ cm. and the other was 3 by $1\frac{1}{2}$ cm. The walls of both were thickened. The lumen was obliterated in the left tube, and in the right tube the lumen was open and contained spongy material and blood. The other tissue submitted was nothing but blood clots.

Ovary measured 4 by 2 cm. in size, congested and rather roughened and irregular. On cut section, one end was occupied by a membrane and fetus which measured about $2\frac{1}{2}$ by $1\frac{1}{2}$ cm. The rest of the ovary was occupied by blood and spongy material. The wall was exceedingly thin.

Under microscopic examination, the left tube showed hyperplasia of the mucosa and the rest of the wall was infiltrated with fibrous connective tissue and round cells. The blood vessels were thickened. The right tube showed decidual cells and chorionic villi in the lumen and the wall was thickened with an infiltration of fibrous connective tissue and round cells. There were minute hemorrhages throughout the wall.

The sections taken from the bloody and spongy portion of the ovary showed the presence of placental tissue with its chorionic villi and decidual cells.

The final diagnosis was (1) right tubal pregnancy, (2) left chronic salpingitis, and (3) left ovarian pregnancy.

In the present case, with the whole fetal sac clearly imbedded in the ovary and the ovary still easily recognizable, there can be no question as to the diagnosis. But to have the left tube uninvolved and chorionic tissue found in the right tube presents a very interesting complication to this case of left ovarian pregnancy. Certainly the clinical study of these cases has contributed very little or nothing to help in elucidating the etiology of this type of atypical nidation.

PHOTOGRAPHY OF THE CERVIX UTERI*

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ALTHOUGH many attempts have been made to photograph the cervix uteri, I have been unable to find any references to the subject in the literature. I have seen a few photographs of this organ, none of which could be termed successful. In most cases drawings have been used to illustrate lesions of the cervix. Proper lighting seems to be the main problem. The usual set-up consists of strong spotlights placed as closely as possible to the camera. It is very difficult to light the entire cervix in this manner, and a further disadvantage is the fact that the light travels practically parallel to the camera lens, thereby producing a very flat picture. The cervix, which is round and has considerable modeling, appears to be all on one flat plane.

Dr. Kimble and I have developed a technic which is new and we believe has several distinct advantages. The essential factor in the success of our work in the photography of the cervix has resulted from the use of a specially designed speculum, of

*Read at a meeting of the Chicago Gynecological Society, May 8, 1936.

LEFT OVARIAN PREGNANCY AND RIGHT TUBAL PREGNANCY

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THE primary reason for reporting this case is that of the extreme rarity of a left ovarian pregnancy complicated by a suspected right tubal pregnancy.

Mrs. G. K., twenty-seven-year-old housewife, was admitted to the Hospital on April 7, 1931. A preoperative diagnosis declared it a case of right-sided ectopic pregnancy. An operation performed on April 11, 1931, under spinal anesthesia, included a left oophorectomy, bilateral tubal resection (partial), dilatation and curettage, and a routine appendectomy.

The final diagnosis was left ovarian pregnancy. On April 25, 1931, the patient was discharged, cured.

The patient's chief complaint consisted of vaginal bleeding, lasting over a period of three weeks, and entailing moderate disability. Associated with the vaginal bleeding the patient experienced abdominal pain, nervousness, exhaustion, mental depression, loss in weight, and constipation.

Her husband is living and well, and she has had one previous normal pregnancy. She is an only child whose father and mother are living and well. There has been no history of chronic diseases in the family. In addition to the usual childhood diseases, she had pneumonia and also a fracture of her right leg.

After the onset of her menses at the age of fourteen, her periods were of the four- or five-day type, occurring every twenty-eight days, with a mild amount of dysmenorrhea. Between periods she had some leucorrhea.

The patient's present illness commenced about three weeks before admission to the hospital, when she began having severe pains in the abdomen and some tenderness. The pains were mainly in the lower abdomen, but occasionally she noticed slight pain in the center of her back. She had some nausea and vomiting, but no eructations of gas. The patient was usually somewhat constipated, necessitating an occasional cathartic. Her constipation was not increased during this illness. At the same time as the onset of her pain, she began to menstruate. This bleeding continued until the time of her admission. She passed several small clots. Previous to this her periods were regular and of four or five days' duration. The date of her last regular period is not given. She had no symptoms of shock, but was very nervous, mentally depressed, exhausted, and began to lose weight. She had no shortness of breath, no precordial pain, and no palpitation. There were no other positive symptoms in any of the other organ systems.

Physical examination showed patient to be a well-nourished and well-developed young female, who did not appear acutely ill and had no special complaints at the time of admission. Blood pressure 130/80. Abdomen not distended and no masses felt. Marked degree of deep tenderness in the lower right quadrant. No rigidity, no fluid. Vaginal examination not done. Temperature 98° F., pulse 80, respirations 20 on admission. Patient was kept under observation for four days. During this time there was a moderate amount of vaginal bleeding, and the patient complained of the same pains previously noted. They were not excruciating, however, and she could be kept fairly comfortable with $\frac{1}{2}$ gr. of luminal, t.i.d.

Urine showed clear, acid in reaction, specific gravity 1.020. No albumin, sugar, acetone, or diacetic acid. Few squamous epithelia and leucocytes, no red blood cells or casts. Blood count revealed a hemoglobin of 54 per cent, with 5,510,000

A NEW, NONIRRITATING OPAQUE MEDIUM FOR UTEROSALPINGOGRAPHY

PRELIMINARY REPORT

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THE injection of iodized oil into the uterus and fallopian tubes for the purpose of x-ray visualization, suggested by Cary in 1921, has been a valuable diagnostic procedure. Its limitation or proper restriction solely to patients in whom small tumors are suspected or tubal obstruction has been demonstrated by means of gaseous insufflation (Rubin test) may still be debated by some. Nevertheless, the fact that sharp chemical reactions with irritative salpingitis and the formation of parametritic masses are not infrequently seen following such injections, argues for a limitation of their use. This has suggested, moreover, that the usefulness of this procedure is impaired by its risks, and that a nonirritating medium would be considerably more satisfactory.

The source of the chemical salpingitis and parametritis frequently initiated by these injections seems to lie in the liberation of free iodine from iodized oil.

Mono-iodomethane sulphonate of sodium (skiodan) in watery solution is entirely nonirritating and has been used extensively in urologic work, but its lack of viscosity made it unsuitable for uterosalpingography. Several different combinations with viscid media were devised in an effort to develop such a solution of the same viscosity as iodized oil. Dextrose, starch, glycerin, propylene glycol, and tragacanth were rejected after animal experimentation showed that for various reasons, to be outlined later, they were unsuitable.

A solution containing 40 per cent of mono-iodomethane sulphonate of sodium (skiodan) in acacia 20 per cent finally proved suitable.* Injections in the tubes of rabbits showed no irritative, histologic changes, and its clinical use has followed thus far with entirely satisfactory results. Moreover, the x-ray pictures seem sharper and clearer than with the iodized oil preparations.

A more detailed description of this preparation, its development, the animal experimentations, and its clinical use is to follow this preliminary report at a later date.

*Suggested and developed by Dr. O. W. Barlow of the Research Laboratories, Winthrop Chemical Company.

a modified, large size, duck billed type, with two special low voltage bulbs mounted in the proximal end of each blade. The inner surfaces of the speculum are of jet black finish, so as to avoid glare from the shiny metal. The bulbs are shaded so as to prevent any light from shining into the lens or from producing undesirable high lights. The lamps are connected to a series of ten flash-light batteries, thereby eliminating the possibility of any serious injury to the patient as a result of electrical shock. The current supply to each bulb is independent of the other, and it is possible to increase or diminish the intensity of each light separately. In this way we are able to control the lighting of our field. For example, in some cases it is best to have the lower light stronger than the upper light or vice versa. In other words, we are able to "model" the cervix with our lights much the same as if the cervix were not an internal organ. With the source of light out of our way, it is a simple matter to set up any camera on a tripod that can be easily and quickly raised or lowered and make the exposure. Most of our pictures have been taken with a 5 by 7 inch clinical camera mounted on an Agfa "Universal" tripod. However, successful pictures have been made with a $3\frac{1}{4}$ by $4\frac{1}{4}$ inch Auto Graflex and a $2\frac{1}{4}$ by $3\frac{1}{4}$ inch Zeiss Icon with a double extension bellows. It is possible to use a Leica camera for this type of work provided a supplementary lens is employed. Lenses of short focal length are preferred in all types of cavity photography. A comparatively short focal length lens permits one to place the camera nearer to the subject; it reduces the exposure time and gives a greater depth of focus. Our pictures are taken about natural size with an average exposure of two seconds at F:8, using Eastman super-speed portrait film and a 6 inch focal length lens. Supersensitive panchromatic film does not produce the best photographs. If the finer details of the cervix are to be brought out clearly, films that are less sensitive in the red end of the spectrum must be used. This is easily explained when we realize that the colors of the tissues of normal and pathologic cervixes are nearly all composed of various shades of red.

High lights on the cervix are quite troublesome. These are due to the mucus which is always present on the surface of the tissue. A powdered mucus digestant called "Alcaroid" may be used to remove this substance, thereby decreasing the intensity of the high lights. A small piece of moist cotton is dipped into the powder and applied directly to the cervix for three to five minutes.

Blurred pictures due to movement of the patient have been few. If the patient holds her breath during the exposure, movement is minimized. We have found the ordinary office surgical examining table with suitable leg rest a very essential part of our equipment. The comfort and ease of the patient must be considered if good photographs are to be produced.

Many conditions of the cervix lend themselves to color photography. Just recently Dr. Kimble and I have made several natural color pictures using the Finlay color process.

The cervix can be photographed best when the lights are placed within the speculum. This method has three distinct advantages. First, the light is not in the way of the camera. Second, the cervix is lighted from a slight angle and as a result modeling is possible. Third, light decreases with the square of the distance it travels; therefore, by placing lights a short distance from the cervix, it is possible to use small low voltage lamps.

REVIEW OF THERAPEUTIC PROCEDURES

1. Elimination.—

Colon Lavage: An essential part of the Rotunda Hospital treatment entails the irrigation of the rectum and colon, using 500 c.c. of warm water at a time and continuing the lavage until a satisfactory evacuation of fecal material has been obtained and the water returns clear. This may require from thirty to sixty minutes and may be repeated every six hours if the convulsions continue or if an anuria develops. This appears to be rather drastic therapy when the same result apparently can be achieved with enemas.

Enemas: The usual soapsuds enemas may be given. Two hundred cubic centimeters of a saturated solution (50 per cent) of magnesium sulphate has been used to dehydrate the patient. It is definitely contraindicated in the presence of a severe oliguria.

Catharsis: The Rotunda Hospital treatment prescribes two ounces of castor oil or three ounces of *misturae sennae compositum* if the patient is conscious. If unconscious, the stomach is washed out with warm water and the purgative injected before the tube is withdrawn.

2. Sedation.—

Morphine³ is given hypodermatically in $\frac{1}{4}$ to $\frac{1}{2}$ gr. doses. Two hours should elapse between injections and no more than 2 gr. should be given in twenty-four hours. One-eighth to one-fourth grain may be given intravenously if the convulsions cannot be controlled with the usual doses, or if the patient is maniacal. If the respiratory rate drops to 10 per minute, no more morphine should be given and atropine may have to be injected.

Morphine, if given in large amounts to animals, produces a rapid and marked acidosis, due to the decreased elimination of carbon dioxide by the lungs. It also causes a concentration of the blood and a decrease in urine volume.

Chloral hydrate is one of the most essential parts of the Stroganoff treatment. If the patient is conscious, 2.0 gm. (30 gr.) are given in milk by mouth. If unconscious, it is given in 100 c.c. of milk by rectum. In either case, it is repeated every six hours, but the dose is decreased to 1.5 gm. (23 gr.). If the convulsions cannot be controlled, these amounts are increased 25 to 50 per cent.

Chloral hydrate is a powerful cardiac depressant and may cause a drop in the blood pressure. The side actions produced by it show considerable resemblance to those of chloroform.

Chloroform is used freely in the Stroganoff treatment. It is a definite liver poison and is now used in very few clinics.

Ether has been given by inhalation to control the convulsions, or 60 c.c. of ether and 120 c.c. of olive oil or mineral oil may be given by rectum. It causes an increased pulmonary secretion and, therefore, if used should be administered with caution.

Magnesium sulphate has been given intraspinally, intravenously, and intramuscularly. The latter two methods are preferable and are as follows:

Intravenous,⁴ 20 c.c. of a 10 per cent solution are injected and repeated every hour until the convulsions are controlled. Occasionally,

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

THE TREATMENT OF ECLAMPSIA

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and The Chicago Lying-In Hospital)*

THE treatment of eclampsia is still unsettled. Some obstetricians advocate medical treatment with a complete disregard of the pregnancy. Some advise the immediate termination of pregnancy, usually by cesarean section, and others advocate a combined medical and obstetric treatment together with individualization of the case. We shall first outline the essential procedures of the various methods of treatment and then describe a combined method which seems to give the best results in many clinics.

Drugs, including the nitrites, croton oil, pilocarpine, etc., and procedures, such as the injection of air into the breasts, nephrotomy, renal decapsulation, dry cupping, hot packs, etc., are used only rarely.

The treatment of eclampsia, in general, has been divided into surgical and medical.

The surgical treatment consists of the immediate termination of the pregnancy by cesarean section, vaginal hysterotomy, or by manual or instrumental dilatation (*accouchement forcé*) of the cervix, followed by version and extraction. The only large clinic, as far as we know, in which eclampsia is still treated by immediate delivery is the Berlin Frauenklinik, supervised by Stoeckel. No recent figures for their maternal mortality are available, but others who practice immediate delivery have reported a mortality rate as high as 23 per cent, and less experienced physicians may have a mortality rate of 48 per cent, as reported in one city.

The medical treatment may be divided into two large groups, as follows:

Stroganoff or Sedation Method¹: Large amounts of morphine and chloral hydrate are administered. Any necessary manipulations are performed under chloroform anesthesia. Venesection and early, but not forcible, delivery through the natural passage are advised.

Rotunda Hospital or Elimination Method²: Colonic irrigation, purgation, starvation, and the parenteral injection of 1 per cent sodium bicarbonate solution are the essentials of the original treatment. The use of morphine and venesection have been added. Labor may be induced only after three days' treatment.

is negligible. He occasionally still uses the procedure. The writer has noted no beneficial results in a small series of patients.

4. Parenteral Fluids.—

Sodium Bicarbonate: Five hundred cubic centimeters of a 1 per cent solution are injected beneath each breast, or intravenously in severe cases, according to the Rotunda Hospital treatment. This solution, as well as normal saline and Ringer's solution are, as a rule, contraindicated in eclampsia because the tissues are usually edematous and, therefore, contain an excess of electrolyte.

Glucose Solution*: Various concentrations are recommended for intravenous injection. Titus and coworkers advise 500 c.c. of a 15 per cent solution, which is injected over a period of thirty minutes and may be repeated two to four times in twenty-four hours. Fay and Arnold give 50 c.c. of a 50 per cent solution every four to six hours. I,⁷ as a rule, give 500 to 1,000 c.c. of a 20 per cent solution over a period of thirty to fifty minutes and repeat it every six to eight hours. In certain cases 300 to 800 c.c. of a 30 per cent solution, or 100 to 200 c.c. of a 50 per cent solution are given.

Two hundred cubic centimeters of a 50 per cent solution of sucrose also has been used. Although our experience is limited, it is no more efficacious than glucose and if the anuria persists, it is potentially dangerous.

The proper use of hypertonic solutions of glucose in pregnancy is one of the outstanding accomplishments of modern obstetrics. The improvement in the maternal mortality rate for eclampsia in the past fifteen years must be attributed in great part to parenteral injections of glucose solution.

5. Spinal Puncture.—This procedure has been tried at various periods and again has been recently advocated by Arnold and Fay. They drain the canal every three to six hours, as is necessary.

6. Dehydration.—The convulsions, coma, hyperpyrexia and various other cerebral and visual symptoms are in all probability caused by an abnormal amount of water in the tissues of the brain. As a rule, there is an edema but all of these symptoms and signs can be produced by an abnormal loss of fluid from the brain. Almost all methods of treating eclampsia have resulted in a negative fluid balance. The most recent method to dehydrate is the Temple treatment which was described by Arnold and Fay⁸ in 1932. They dehydrate their patients by repeated spinal drainage, by magnesium sulphate solution given intravenously and by mouth or rectum, by intravenous hypertonic glucose solution, by venesection and starvation. The fluid balance is regulated so that it is negative. Dehydration was used in the nineties to control the convulsions of eclampsia and uremia but was discontinued. While the present method is a tremendous improvement over the old one, the results are no better than those achieved with other methods. It has been our experience that ~~that~~ excessive restriction of fluid and very large doses of magnesium sulphate as a purgative have occasionally seemed to make the toxemic patient worse.

7. Diet.—During the eclamptic attack, nothing should be given by mouth. Complete starvation for at least three days is part of the Rotunda Hospital treatment.

*Solutions in 500 to 1,000 c.c. amounts for parenteral injection are prepared by various concerns and readily available through medical supply houses in almost all large cities.

the injection of 100 to 200 c.c. of a 2 per cent is more efficacious than the 10 per cent solution, especially in a patient with hypertensive encephalopathy.

Intramuscular, 15 c.c. of a 25 per cent solution are injected deep into the gluteal muscle and 15 c.c. are given after each convulsion until controlled. As much as 200 c.c. has been administered in twenty-four hours.

Magnesium is eliminated chiefly by the kidney. Therefore, if an anuria or even a severe oliguria is present, magnesium is retained in the blood and may reach a concentration at which coma ensues and death may result.

Barbiturates.—Sodium amytal⁵ may be given intravenously as a 10 per cent solution. The rate of injection is 1 c.c. per minute. Five to ten cubic centimeters, 0.5 to 1.0 gm. ($7\frac{1}{2}$ to 15 gr.) may be necessary to control the convulsions; then 0.2 gm. (3 gr.) is given every four hours either by mouth or rectum.

Luminal sodium or phenobarbital sodium, 0.12 to 0.3 gm. (2 to 5 gr.) can be given subcutaneously or intravenously.

Nembutal or pentobarbital sodium,⁶ 0.5 gm. ($7\frac{1}{2}$ gr.) may be dissolved in 10 c.c. of sterile water and 4 to 8 c.c. given intravenously at the rate of 1 c.c. per minute; 0.6 to 0.8 gm. (6 to 8 capsules of $1\frac{1}{2}$ gr. each) is given in addition by rectum. Ten or 12 capsules may be given alone by rectum. If convulsions recur or restlessness appears, 3 to 6 capsules may be given and repeated in twelve hours, if necessary.

The barbiturates, if given intravenously to animals, stop convulsions, produce muscular relaxation, induce sleep, and lower the blood pressure. The latter effect is usually only temporary, but it may be so marked and prolonged that an anuria or oliguria results. They produce a slight increase in the carbon dioxide content of the blood and a fall in the pH, that is, a slight and temporary acidosis is produced. A slight blood dilution occurs, but in view of the marked increase in weight and volume of the spleen, the dilution is apparently not a true one but is due to a withdrawal of cells by the spleen. Large amounts of the barbiturates are certainly contraindicated. McGee reports that when amytal was given intravenously in eclamptics, it lowered the blood pressure to such a degree that an anuria was produced. Ephedrine sulphate had to be given to raise the blood pressure to produce a secretion of urine.

3. Venesection.—The withdrawal of 300 to 1,000 c.c. of blood is still practiced in some clinics. The results of treatment indicate that venesection is not essential, providing other procedures can be carried out. Furthermore, it cannot be performed very often; only one venesection may produce an anemia of such a degree that, if there is excessive blood loss during delivery, infection may occur because of lowered tissue resistance or death may result from the anemia. The eclamptic patient is not plethoric. The average hemoglobin is 14.9 gm. per 100 c.c. of blood. This figure, which is high for the pregnant individual, is the result of the blood concentration. After delivery the hemoglobin will drop 10 to 40 per cent.

Irving has substituted plasmapheresis for venesection. One thousand cubic centimeters are drawn into a sterile bottle containing sodium citrate. Under aseptic conditions the cells are separated from the plasma and reinjected into the patient. The loss of hemoglobin

	MATERNAL MORTALITY—%	
	MILD	SEVERE
Natural delivery	4.5	36.9
Assisted delivery	5.6	31.7
Induction of labor	6.6	26.4
Cesarean section	11.3	46.3
Accouchement forcé	18.1	63.1

It is obvious that the mortality rate for the mild cases is markedly increased by any procedure which carries its own mortality. In contrast, the severe cases carry a very high mortality rate and any procedure which hastens delivery without any high inherent mortality of its own increases the patient's chances for recovery. The conclusion is obvious that severe eclampsia is best treated by early delivery.

Many obstetricians have stated that it is difficult, if not impossible, to classify the type of eclampsia early enough to be of value. At the Chicago Lying-In Hospital we classify the severe type by the presence of one or more of the following findings:

1. Coma.
2. Temperature of 102° F. or more.
3. Pulse rate over 120.
4. Respiratory rate over 35.
5. More than 10 convulsions.
6. Cardiovascular impairment (edema of the lungs, persistent cyanosis, low or falling blood pressure, low pulse pressure, etc.).
7. Failure of our treatment to:
 - (a) Stop the convulsions or prevent their recurrence.
 - (b) Produce a urinary output of at least 700 c.c. per twenty-four hours.
 - (c) Prevent the onset or increase in degree of coma.
 - (d) Produce a dilution of the blood as indicated by a decrease of at least 10 per cent in hemoglobin, cell volume or serum protein concentration.

With these criteria and the knowledge of what our treatment should accomplish, we can frequently classify the type of case on admission or within six to eight hours. If the case is severe arrangements are made to terminate the pregnancy by the easiest and safest method.

COMBINED METHOD OF TREATMENT (CHICAGO LYING-IN HOSPITAL)

The treatment which is used at the Chicago Lying-In Hospital¹⁰ and which, with perhaps minor changes, is used in many other clinics, may be termed the "combined method" because the essential parts of the various methods have been systematized for certain definite purposes.

GENERAL TREATMENT

The patient is placed in a quiet, cool, darkened room. Constant observation is necessary to prevent injury to the tongue, falling out of bed and aspiration of vomitus or drowning from the occasional excessive pulmonary secretions. A mouth gag (clothes pin, tooth brush) and tracheal catheter should be at hand. A catheter should be kept in the bladder until the patient is definitely improving. The temperature, pulse and respiratory rate, urine volume, and blood pressure should be determined every two hours until the patient is conscious and improving. The period is then lengthened to four hours

8. *Veratrum Viride*.—Very few clinics, as far as we know, still treat eclampsia with this drug. Gillespie,⁹ some years ago, described its use as follows: Sixty minims of veratrone are given on admission, and 15 minims every ten minutes until there is sighing respiration, copious vomiting, which should last for at least two hours, and a soft pulse with a rate of 40 to 60 per minute. Anderson states that at the Glasgow Royal Maternity Hospital they give 0.5 c.c. (7½ minims) of veratrone if the systolic blood pressure is over 160. They never repeat the injection because of the possibility of shock developing. This drug is a powerful cardiac depressant. Bailey and Schwarz each stated that when the use of the drug was popular many patients went into vascular collapse or shock after its administration and some deaths were undoubtedly attributable to it.

9. *Pregnancy*.—It is an incontrovertible fact that the products of conception (placenta and/or fetus) are responsible in some way for the eclampsia, and that the earlier they are removed the better chance the patient has of surviving. Mortality reports, some of which are given in Table I, indicate that surgical treatment, almost without exception, results in an appallingly high death rate. Likewise, if medical treatment is used and no attempt is made to terminate the pregnancy, especially in the severe cases, the mortality rate is also very high. However, the radical surgical method in inexperienced hands gives a mortality rate which is two or three times as great as the radical medical method in the same hands. It is obvious that there is a middle course. Careful observations in many clinics indicate that the medical treatment, together with early but not forcible termination of pregnancy, gives the best results.

Eden and coworkers have stated that the patients with eclampsia could be classified as mild or severe, depending on certain symptoms. They stated that the case was severe if two or more of the following findings were present: Coma, temperature over 103° F., pulse rate over 120, more than 12 convulsions, blood pressure over 200, no edema and the urine solidifies on heating.

Eden classified 706 patients who had been treated by various physicians.

AUTHOR	COUNTRY, STATE OR CITY	YEAR OF REPORT	NUMBER OF ECLAMPTIC PATIENTS	MORTALITY PER CENT		TREATMENT
				MATERNAL	FETAL	
Peterson	U. S. A.—collec- tive	1914	283	25.8		Radical surgical
Davis and Harrar	New York	1926	495	23.7		Radical surgical
Kontsek	Germany	1931	117	18.0	16.0	Radical surgical
Williams	Baltimore, Md.	1912	110	22.8	57.6	Radical surgical
Miller and King	New Orleans, La.		138	38.8		Radical surgical
Zweifel	Germany	1923	394	18.5		Radical surgical
Placc	All—collective	1927	4607	21.7		Radical surgical
Upshaw	Atlanta, Ga.	1932	91	5.4	25.9	Combined
Dorsett and Dieckmann	St. Louis, Mo.	1929	186	7.0		Combined
Williams	Baltimore, Md.	1927	165	13.3	56.6	Combined
Miller and King	New Orleans, La.		38	15.8		Combined
Zweifel	Germany	1923	317	8.5		Combined
Placc	All—collective	1927	5976	11.1		Combined

of cardiac failure, 300 to 500 c.c. of a 30 per cent, or 100 to 200 c.c. of a 50 per cent solution are given. We have never seen any injurious effects if the glucose solution is properly prepared and administered.

PREGNANCY

While the various procedures outlined above are being carried out, the period of gestation, size of fetus, and irritability of the uterus are determined. No attempt to start labor or terminate the pregnancy should be instituted until the eclampsia is under control, which usually requires six to ten hours.

Antepartum and Intrapartum Eclampsia.—If there is cephalopelvic disproportion, a cesarean section should be performed when the eclampsia is under control. This presupposes that the case is not actually or potentially infected.

Severe Eclampsia—Over 35 Weeks' Gestation: If there is no disproportion and if the cervix is effaced and soft, labor should be induced by rupturing the membranes, care being taken to drain off as much of the amniotic fluid as possible, and, if necessary, inserting a bag. Pituitrin in doses of one or two minims or preferably pitocin may be given subcutaneously every thirty minutes until the interval between contractions is two or three minutes and the duration of each is forty to fifty seconds. But if the cervix is long, firm and closed, a cesarean section should be performed if the environment is suitable.

Severe Eclampsia—Under 35 Weeks' Gestation: The cervix will, as a rule, be uneffaced, firm and closed. In general, labor should be induced as described in the preceding paragraph.

Mild Case—Any Period of Pregnancy: No operative procedure should be carried out. Labor should be induced only if the cervix is soft and partly dilated. If the patient is not delivered, she must be kept under close observation until the pregnancy is terminated, because if the eclampsia recurs it is usually of the severe type and is quite often fatal.

Postpartum Eclampsia.—The treatment is entirely medical.

DIET

If the patient is conscious or as soon as the stomach is emptying itself, as indicated by a failure to aspirate water which has been previously injected, a 10 per cent solution of Karo syrup is injected through the nasal tube at hourly intervals. The initial amount is 50 c.c. and is increased by 50 c.c. amounts up to the patient's tolerance (usually 200 to 300 c.c.). These feedings are continued until the patient is able to take the eclamptic diet which consists of water, fruit juices and fruit. The fluid balance must be watched carefully and kept negative.

MISCELLANEOUS PROCEDURES

The withdrawal of 500 to 1,000 c.c. of blood may be necessary if acute cardiac failure and pulmonary edema develop. Spinal puncture is rarely if ever indicated and then only if there are signs of a markedly increased intracranial pressure. The blood pressure should be watched carefully. Occasionally it drops before delivery and may require treatment. After delivery a 10 to 15 pound weight (sand bag) should be placed on the abdomen and a tight binder applied for eight to twelve hours to prevent vasomotor collapse. If the latter

and later the intervals are increased still further. The patient's condition as to the number of convulsions, the degree of coma, the quality of the pulse, difficulty in breathing, cyanosis, etc., should be noted.

CONVULSIONS

Since all drugs are toxic in the doses necessary to control the convulsions, we prefer to use several simultaneously. Smaller amounts are, therefore, required and the undesirable effects of each are minimized. A number of hypnotic drugs are mentioned because all are not always available. We prefer magnesium sulphate and luminal sodium. If the case is protracted, chloral hydrate is used.

Morphine.—One-fourth grain is given on admission and repeated at hourly intervals until the convulsions are controlled or the respirations drop to 10 per minute.

Magnesium Sulphate.—Ten cubic centimeters of a 25 per cent or equivalent amounts of a 50 per cent solution are injected and 5 c.c. of the former solution are given after each convulsion or until a total of 30 c.c. has been given.

Luminal Sodium.—Three-tenths gram (5 gr.) is injected subcutaneously and, if necessary, it is repeated in twelve to twenty-four hours.

Chloral Hydrate.—Two grams (30 gr.) are given in 100 c.c. of starch water (one tablespoonful of starch to 100 c.c.) by rectum and repeated as necessary.

ELIMINATION

A soapsuds enema is used and should be repeated until a satisfactory bowel movement has been obtained. If the patient is vomiting the stomach is emptied with a nasal tube but no cathartic is injected. Sodium sulphate (Glauber's salt), 30 to 45 gm., is a safer purgative than magnesium sulphate.

HYPERTENSION

The blood pressure, at least in part, is compensatory. All sedative drugs lower it, but the barbiturates and chloral hydrate are the most efficacious in reducing it or in preventing further increases.

RENAL AND CEREBRAL SYMPTOMS

The oliguria or anuria, coma, fever, tachycardia and cerebral edema are treated with injections of hypertonic glucose solution. Five hundred to 1,000 c.c. of a 20 per cent solution are given intravenously over a period of thirty to fifty minutes and this amount is repeated every six to eight hours, if necessary. The temperature of the solution at the needle point must be 100° F. This can be achieved by immersing at least three feet of the rubber tubing in water at a temperature of 104 to 106° F. Within four hours after the injection the urine volume should equal at least 60 per cent of the volume injected. Sufficient glucose solution is given to insure a urinary output of at least 30 c.c. per hour and should be continued during the postpartum period until the normal diuresis begins. If the 20 per cent concentration does not produce a diuresis, 500 to 800 c.c. of a 30 per cent solution are used. If there is an anasarca or if there are symptoms

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

GYNECOLOGIC OPERATIONS

Jonas, Emil: Simplified Technique of Abdominal Supravaginal Hysterectomy, Illinois M. J. 68: 347, 1935.

The author lists 6 positions where fibromyomas may be found when the peritoneum is opened. Each position necessitates a slight modification in the technic, which is as follows: one clamp is placed on the insertion of the round ligament into the uterus. A No. 1 chromic catgut suture is placed laterally to the clamp, and the ligament cut between clamp and suture. The process is repeated on the fallopian tube and the ovarian ligament, bilaterally. Each suture is left long and held by a separate forceps. The sutures are now raised so that the two layers of the broad ligament can be separated. The anterior layer on each side is cut downward in the direction of the cervix, keeping close to the uterus. The bladder is pushed away and a transverse incision is made on the anterior layer from one side of the cervix to the other. The uterus is delivered through the abdominal opening by means of traction forceps and the bladder elevated with a narrow retractor. A cut corresponding to that made in the anterior layer is now made in the posterior layer of the broad ligament, and the terminal cut ends are pushed downward, exposing the uterine vessels. These are now ligated as follows: using No. 1 chromic catgut and a cervical needle two mass sutures are taken into the cervical tissue one-half inch apart and one-half inch from the cervix. The long ends of these sutures are tied on the anterior wall of the cervix. Another ligature, carried by an aneurysm needle, is placed between these two sutures. A transverse cut now amputates the cervix. Usual treatment of the stump and peritoneum follows.

EUGENE S. AUER.

Loute, L.: Systematized Ligamentopexy in Conservative Gynecology, Presse méd. 84: 1628, 1935.

The physical factors responsible for the maintenance of the normal position of the uterus are reviewed, and the mechanism of acquired retrodisplacements of the organ is discussed.

The author presents his modification of the round ligament shortening operation by Doléris, and advocates the method for correction of either existing retrodisplacement or as a routine procedure in any conservative gynecologic operation to prevent future displacements.

Technic: Pfannenstiel incision. The round ligaments are cut laterally at their entrance into the internal inguinal ring and the distal segment is ligated. Each

occurs, ephedrine ($\frac{3}{4}$ gr.) every two to four hours, hypertonic glucose solution and occasionally blood transfusions are necessary. Atropine in doses of $\frac{1}{100}$ gr. should be given if there are many râles. Up to $\frac{1}{30}$ gr. may be given within one hour if pulmonary edema occurs. Oxygen should be administered by nasal catheter if the patient is cyanotic.

ANESTHESIA

Operative procedures can be performed quite often without any additional anesthesia because of the large amounts of narcotics already given. If additional anesthesia is necessary, local infiltration with novocaine solution is preferable.

REFERENCES

- (1) *Stroganoff, W.*: The Improved Prophylactic Method in the Treatment of Eclampsia, Wm. Wood & Co., New York, 1930. (2) *Solomons, B.*: Tweedy Practical Obstetrics, Oxford Medical Publication, ed. 6, 1930. (3) The American Committee on Maternal Welfare, J. A. M. A. 104: 1703, 1935. (4) *McNeile, L.*: J. A. M. A. 103: 548, 1934. (5) *King, E., Mayer, G., and Ayo, T.*: AM. J. OBST. & GYNEC. 23: 867, 1932. (6) *Ross, J.*: AM. J. OBST. & GYNEC. 31: 120, 1935. (7) *Schwarz, O., and Dieckmann, Wm. J.*: AM. J. OBST. & GYNEC. 18: 515, 1929. (8) *Arnold, J., and Fay, T.*: Surg. Gynec. Obst. 55: 129, 1932. (9) *Gillespie, Wm.*: Therapeutic gaz. 47: 457, 1923. (10) *Dieckmann, Wm. J.*: Surg. Gynec. Obst. 59: 678, 1934.

Society Transactions

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MAY 7, 1936

The following papers were presented:

Ovarian Rupture Causing Intraperitoneal Hemorrhage. Dr. S. Leon Israel (by invitation). (For original article, see page 30.)

A Consideration of Lumbosacral Spina Bifida Occulta With Special Reference to Uterine Prolapse. Dr. George M. Laws. (For original article, see page 126.)

Some Remarks Concerning the Use of Internal Podalic Version in Obstetrics. Dr. George Ulrich.

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MAY 8, 1936

The following papers were presented:

Photography of the Cervix Uteri. Dr. Ralph H. Creer and Dr. H. E. Kimble. (For original article, see page 162.)

Vascular-Renal Effects of Posterior Pituitary Extracts in Pregnant Women. Dr. William J. Dieckmann and Dr. Herbert L. Michel. (For original article, see page 131.)

Evipal Soluble Anesthesia in Gynecology. Dr. Herbert L. Schmitz. (For original article, see page 102.)

Clinical Observations on the Effect of 800 K. V. Roentgen Rays in Uterine Carcinomas. Dr. Henry Schmitz. (For original article, see page 74.)

Evaluation of Salpingostomy and Tubal Implantation for the Treatment of Sterility. Dr. J. P. Greenhill. (For original article, see page 39.)

Koller: Hydrosalpinx Following Sterilization by Crushing and Ligation of Uterine Tubes, *Arch. f. Gynäk.* 155: 185, 1935.

The author describes three instances in which hydrosalpinx resulted from sterilization operations by crushing or ligating the tubes. In one patient both methods were used. He believes that sterilization operations should be preceded by careful temperature, leucocyte and sedimentation time controls to rule out any possibility of existing infection, and that no operation should be performed until all tests are found normal. The sterilization should never be performed until at least eight weeks have elapsed since delivery, abortion, or fever. A longer period should be allowed if pelvic thromboses or pelvic infection has been present.

The method of sterilization should be as simple as possible. All stumps and all tissues with impaired circulation should be extraperitonealized. The author now uses subperitoneal resection of the tubes without ligation, followed by peritonealization. He recommends using only the isthmic portions of the tubes because this will prevent either immediate hydrosalpinx formation or ascending infection with subsequent hydrosalpinx. Any evidence of tubal infection or inflammation at the time of operation requires tubal resection rather than sterilization by any form of tubal ligation.

RALPH A. REIS.

Runge, H.: Disturbances Following the Removal of One Ovary, *Monatschr. f. Geburtsh. u. Gynäk.* 100: 233, 1935.

It is ordinarily believed that during the course of an operation, we may safely remove one ovary without concerning ourselves about subsequent disturbances. However, it is the opinion of Runge that trouble arises more frequently than is realized. He instituted a follow-up of 345 women who had only one ovary removed. Of this number 196 were traced. In the majority of instances the original diagnosis which necessitated removal of one ovary was either chronic inflammatory disease or ectopic pregnancy. In order to determine whether the remaining ovary suffered from removal of the other ovary, a study was made of disturbances in menstruation following the operation. Regular menses as before the operation 52 per cent, improved menses 13 per cent, unchanged menstrual periods 4 per cent, more frequent periods 7 per cent, less frequent periods 2 per cent, diminished flow 9 per cent, increased flow 5 per cent, and amenorrhea 3 per cent. Cystic degeneration of the remaining ovary was found in 15.5 per cent of the cases. Whereas in severe instances, ovarian cysts are the result of adhesions around the ovary with prevention of follicle rupture this is by no means true of all cases. Furthermore, not all cases of cystic ovary are associated with menstrual disturbances. Even pregnancy may occur in the presence of a cystic ovary. The practical lesson from this study is that for undisturbed genital function to occur, both ovaries are essential.

J. P. GREENHILL.

Dieulafoy, R.: Conservation of the Uterus After Bilateral Oophorectomy and the Question of Uterine Hormones, *Rev. franc. de gynéc. et d'obst.* 31: 21, 1936.

The author is of the firm opinion that numerous clinical facts show that conservation of the uterus even after both ovaries are removed is far from illogical because it frequently prevents the appearance of menopausal symptoms which usually follow castration. Histologic and experimental investigations show that the uterus has an internal secretion. Furthermore, the anatomic situation of the uterus helps in maintaining the physiology of the small pelvis. The author be-

rectus muscle is perforated with forceps obliquely at the level of the internal ring through the middle inguinal fossa about a centimeter medial to the deep epigastric artery. With forceps the free ends of the round ligaments are drawn through the oblique tract and sutured to each other in front of the recti. Abdominal wall closed in usual manner.

Following advantages are stressed: Simple operative technic based upon anatomic and physiologic principles, with practically no operative risk; good immediate and remote results (checked by pelvic examinations and hystero-graphy); no detrimental effect on fecundity, pregnancy, delivery or postpartum state.

ARNOLD GOLDBERGER.

Thomä, E.: The Alexander-Adams Operation. Results of an Investigation of 200 Operations, Monatschr. f. Geburtsh. u. Gynäk. 103: 49, 1936.

In a series of 200 Alexander-Adams suspension operations the author reports recurrences in only 1 per cent as far as the anatomic results were concerned. Concerning functional results, the operation was a success in 91 per cent of the cases. Only 2.5 per cent of the patients actually claimed they were not helped by the operation. There was only 1 abdominal hernia in this series. Pregnancy followed in 13.5 per cent of these patients and complications did not occur in a single one during labor.

J. P. GREENHILL.

Sigwart, W.: Ventral Suspension of the Uterus and Its Permanent Results, Monatschr. f. Geburtsh. u. Gynäk. 102: 286, 1936.

The author claims the following advantages for his operation for ligament suspension of the uterus: There is no danger of ileus. The uterus is placed both in a practical and physiologic position. Other disturbances do not occur and during subsequent pregnancies and labors there are no complications. There are no disturbances as a result of the fixation of the round ligament.

J. P. GREENHILL.

Goulart de Andrade, Claudio: The Treatment of Prolapse of the Uterus by Halban's Operation, Rev. de gynec. e d'Obstet. (Rio de Janeiro) 29: 631, 1935.

The writer reports in detail two cases of complete prolapse of the uterus operated by a modified Halban's technic which in his belief proves highly satisfactory for this type of case.

F. L. ADAIR AND J. SUAREZ.

Brandt, T.: A Tubo-Uterine Method of Permanent Sterilization, Acta obst. et gynec. Scandinav. 16: 160, 1936.

In the author's method of producing permanent sterilization in women he first places a ligature about 1 cm. below the uterotubal junction on each fallopian tube. This affixes the tubes to the uterus. He then proceeds to make the usual uterotubal excision and closes the wound in the uterine corner with two Lembert stitches. The raw surface is then completely peritonealized with the round ligament although this part of the operation is not essential. The operation can readily be performed in three minutes, it is bloodless, and the results according to the author are excellent.

J. P. GREENHILL.

Jayle, F.: *Esthetics in Laparotomies*, *Compt. rend. Soc. franç. de gynéc.* 5: 269, 1935.

The ideal for a surgeon is to leave behind an invisible signature of his surgical performance. In most instances where a median abdominal incision is employed, about two-thirds of the incision is later hidden by the pubic hair, provided there is an abundant growth of hair. However, Jayle makes a plea for the Pfannenstiel transverse abdominal incision because it is the most esthetic of all.

J. P. GREENHILL.

Mahoney, Louis E.: *Prevention of Gas Pains*, *Am. J. Surg.* 32: 272, 1936.

Gas pains are the most distressing postoperative complication. Proper preparation of patient and extremely gentle operative manipulations are very important.

Ordinary postoperative treatment and usual dietary regime predispose to gas formation. Hospital liquid diet is semistarvation and causes proliferation of putrefactive and gas-forming bacteria. Liquid diet is to be avoided and water and solid food given at once. Mineral oil is prescribed and enemas are avoided.

The results of such technic are good appetite, no gas pains, bowel movement on the third day, very little loss of weight, and earlier return to work.

J. THORNWELL WITHERSPOON.

Ulrich, B.: *Emboli Occurring After Operations Performed Through the Vaginal Route*, *Compt. rend. Soc. franç. de gynéc.* 6: 120, 1936.

Postoperative embolism remains as one of the most disagreeable problems for the gynecologic surgeon. However, the author points out that the risk of embolism after operations through the vagina is extremely small. Gynecologists agree that 75 per cent of all postoperative emboli occur after operations for uterine fibroids, and in most instances without preliminary phlegmasia alba dolens. The only instance of embolism after a vaginal operation, a hysterectomy, was reported by Fournier. One of the most important reasons for the infrequency of emboli after vaginal operations is the lack of operative shock, though shock not infrequently follows abdominal operations and is due to a number of causes. Among them are long duration of the operation, long inhalation anesthesia, Trendelenburg position, and extensive and frequent brusque instrumental and digital manipulations in the abdominal cavity. On the other hand, vaginal operations may be performed very quickly without a general anesthetic and with a minimum of manipulation. Furthermore, there is far less risk of infection with a vaginal operation.

J. P. GREENHILL.

Hristu, C.: *Vaccino-Therapy and Avoidance of Drainage*, *Bull. Soc. d'obst. et de gynéc.* 25: 43, 1936.

During the past seven years the author has not resorted to drainage. He builds up the patient's resistance by vaccinotherapy. He vaccinates his patient for a month before the operation. At the time of laparotomy he removes the appendix prophylactically. He is particularly careful that all bleeding is checked and routinely gives vaccines after operation. In 1935 he reported a series of 500 successful appendectomies without drainage.

J. P. GREENHILL.

lieves that a healthy uterus or one even slightly inflamed should be retained even if a woman has passed her sexual life. The uterus, however, should be fixed in place to prevent retroflexion or descensus.

J. P. GREENHILL.

Lindner, G.: Conservative Treatment or Operation for Chronic Adnexal Disease, *Monatschr. f. Geburtsh. u. Gynäk.* 102: 216, 1936.

The author investigated the results of treatment in 611 cases of adnexal disease. He found that the end-results of conservative operations were inferior to those of nonoperative conservative treatment. However, conservative therapy requires a longer time and usually more than one course of treatment must be administered over a period of many weeks. If conservative treatment does not help the patient or if severe pain persists, then a radical operation should be performed regardless of the patient's age and her desire for children.

J. P. GREENHILL.

Baumgart, E.: The Question of Radical Operation for Chronic Adnexal Disease, *Monatschr. f. Geburtsh. u. Gynäk.* 102: 149, 1936.

Baumgart is of the opinion that in spite of strenuous efforts with conservative therapy and in spite of repeated conservative operations, many women with chronic adnexal inflammation have recurrences which keep them in ill health for many years. These patients become free of symptoms only when, in spite of their youth, a radical operation is performed. Hence the author advises that if conservative treatment does not help a patient with adnexal disease, and an operation is to be performed, the operation should be a radical one, even when the ovaries are not badly diseased. In these young women the author failed to observe menopausal symptoms after radical operations.

J. P. GREENHILL.

Björkenheim, Edv. A.: A Case of Malignant Tumor of the Ovary of Mesenchymal Origin in a Six-Year-Old Girl, *Finska läk.-sällsk. handl.* 78: 49, 1935.

Björkenheim reports a case of malignant tumor of the ovary of mesenchymal origin in a girl six years old. A unilateral oophorectomy was done.

The history presents a child apparently normal at birth who at the age of four years showed enlargement of breasts with pigmentation of areolae. Severe vaginal bleeding had occurred on two occasions. A tumor of the right ovary about the size of a baby's head was removed at operation. A very detailed report of the microscopic studies follows, together with a review of the statistics, the incidence of primary sarcoma of the ovary being placed at 1.6 per cent to 7.5 per cent by the various authors.

A follow-up two years after operation found the patient well and attending school.

E. C. ANDREASSEN.

Kanter, A. F.: Congenital Absence of the Vagina, *Am. J. Surg.* 30: 314, 1935.

The author describes a simplified operation for making an artificial vagina. A small transverse incision is made across the hymen and by blunt dissection the bladder is separated from the rectum. This cavity is then packed. The cavity is dilated, douched and repacked at regular intervals. Within two to three months this cavity will be completely lined with epithelium, the origin of which probably is the hymen.

J. THORNWELL WITHERSPOON.

- South Bend*
BICKEL, D. A.
- Iowa**
Cedar Rapids
BROWN, W. E.
Iowa City
MENGERT, W. F.
PLASS, E. D.
RANDALL, J. H.
Sioux City
CROWDER, R. E.
- Kansas**
Kansas City
SIMS, T. J., JR.
Wichita
COWLES, G. E.
WEST, R. A.
- Kentucky**
Lexington
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TO DATE, SEPT. 1, 1936

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NOTE.—For complete biographic details including age, color, time and place of graduation, date of license, special practice, society membership, etc., reference should be made to the American Medical Directory when using the above list.

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<i>Washington</i> RUBEN, SAMUEL, A.	<i>Virginia</i> <i>Newport News</i> PAYNE, WAVERLY R.	<i>Syria</i> <i>Beirut</i> DORMAN, H. G. Total_____ 611

American Board of Obstetrics and Gynecology

The written examination for Group B applicants will be held in the various cities throughout the United States and Canada on Saturday, March 6, 1937, at 2:00 P.M. Practical oral, and clinical examinations for Group A and B applicants will be held at Atlantic City, N. J., on June 7 and 8, 1937.

Applications must be received at least sixty days prior to the examination dates. Secretary: Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa.

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cine. By the end of the nineteenth century, well-established Women's Clinics were functioning in several countries, many combining gynecology with obstetrics in both teaching and practice. In Great Britain, Germany and Austria, combined departments, under the guidance of departmental heads well grounded in both branches of the specialty, were created, thus placing the teaching of diseases of women on a sound basis. In France, however, gynecology and obstetrics were distinctly separated, as they are today, the teaching of the former being in the hands of general surgeons, who, when appointed to the chairs of gynecology, limited their instruction and practice to that art.

In America several physicians made noteworthy contributions to the development of the science and art of gynecology. The names of Ephraim McDowell, J. Marion Sims, Robert Battey, Nathan Bozeman and many others are familiar to all practitioners and medical students and recall to mind the importance of their original work. Ephraim McDowell opened the door to abdominal surgery, and the story of Jane Crawford has been told and retold in the classroom and before medical societies. To J. Marion Sims we owe a debt of gratitude for conquering a distressful malady, vesicovaginal fistula, and even to this day the technic which he so carefully developed is employed unchanged in the treatment of a number of these disorders. Following Sims in the Woman's Hospital in the State of New York, Thomas Addis Emmet presented to the world the principles of vaginal plastic surgery. Robert Battey, of Rome, Georgia, proposed his operation of removing the ovaries to "establish at once the change of life for the effectual remedy of certain otherwise incurable maladies." This operation was a source of controversy from the beginning, and may have helped to settle the point that normal ovaries should not be removed. The brothers, John Light Atlee and Washington Lemuel Atlee, played an important part in American gynecology. Washington Atlee was awarded the prize of the American Medical Association for the year 1853 for his paper entitled "The Surgical Treatment of Fibrous Tumors of the Uterus, Heretofore Considered Beyond the Resources of Art."* On Jan. 5, 1861, the Obstetrical Society of Boston was organized. This society, the oldest in our specialty in this country, has held continuous meetings since that date or for seventy-five years. The American Gynecological Society was founded in 1876 and the American Association of Obstetricians and Gynecologists in 1888, this organization becoming the American Association of Obstetricians, Gynecologists and Abdominal Surgeons in 1920. The progress of American gynecology is well depicted in the transactions of these two National Societies.

In North America the tendency of the present is to unite the two specialties in a woman's clinic. This ideal situation is becoming more and more apparent in educational centers, such as the university hos-

*Trans. A. M. A., vol. 6, 1853.

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No. 2

American Association of Obstetricians, Gynecologists
and Abdominal Surgeons*

UNDERGRADUATE TEACHING OF GYNECOLOGY IN NORTH AMERICA

PRESIDENTIAL ADDRESS

LOUIS E. PHANEUF, M.D., Sc.D., F.A.C.S., BOSTON, MASS.

THE specialty of gynecology has gone through three different phases. It was at first attached to medicine, then to surgery, and it is now coordinated with obstetrics. The Greek conception of the teaching and practice of medicine had a tendency toward unification: thus, Hippocrates taught and practiced both medicine and surgery. The Arabs owed their success in the sciences to the Greek authors, whose writings they translated and whose traditions they followed. With the migration of the center of medical education to occidental Europe, the physicians abandoned the practice of surgery to the surgeons and barbers. During the thirteenth century physicians and surgeons again appropriated all the branches of medical practice. Diseases of women, the therapeutics of which were medicosurgical, were treated by all. In France, Récamier, although a physician, practiced uterine curettage, amputation of the cervix, and vaginal hysterectomy.

After the discoveries of Pasteur and Lister the surgeons took over the practice of gynecology to a great extent, and justly profited by the impetus and improvement which they contributed to this branch of medi-

*All papers published in this issue up to page 342 were read at the Forty-Ninth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, held at Bretton Woods, N. H., September 14 to 16, 1936.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

1796, there are no facilities for housing patients except for diagnosis. This is one of the large out-patient clinics of Boston. In 1934 there were 2,209 gynecologic patients making a total of 8,928 visits. Of this group only 84 or less than 4 per cent were recommended to hospitals for operation. In 1935, 2,103 patients made 7,117 visits and 71 patients, slightly more than 3 per cent, were referred for operative procedures. While it is true that in hospitals having a House Service a larger number of patients may be sent in for surgical intervention, these figures tend to show, nevertheless, that the majority of patients with gynecologic complaints may be treated by conservative means. At our 1929 meeting, Walter T. Dannreuther, in his paper entitled "The Teaching of Postgraduate Gynecology," stated that in the year 1928, at the gynecologic clinic of the New York Postgraduate Medical School and Hospital, 2,864 new patients had been seen, of which 228, about 8 per cent, had been operated upon. In view of the foregoing, one cannot help but feel that conservative therapy, even though prolonged over a considerable period of time, is more skillful treatment than castration by hysterectomy, and will certainly react to the advantage of the patient in most instances.

The American Board of Obstetrics and Gynecology, the foundation and function of which formed the subject of Dr. Dannreuther's presidential address in 1932, has done and is doing a great deal to elevate the standards of our specialty in this country. Examinations conducted by this board have shown that education in gynecologic and obstetric pathology has been sadly deficient in our American medical schools, and a not uncommon statement by candidates for the board's examination is that they have not looked at a microscopic slide since they left the medical school.

Fred L. Adair, writing on obstetric education in the report of the Sub-Committee on Obstetric Teaching of the White House Conference, states:

There are relatively few places where additional training in obstetrics can be secured. Such opportunities exist mostly in the large cities in connection with maternity hospitals. Usually such hospitals have not had close connection with medical schools.

What is said about obstetrics applies equally to gynecology. Many of the large hospitals in America have no separate gynecologic service or woman's clinic, the gynecology being assigned to general surgery. In the presence of this condition, it is evident that patients, for the teaching of our specialty, cannot be grouped and used to advantage to the patient, the student, and the teacher. By segregating these patients on a separate service, on the other hand, the methods employed for their care can be better demonstrated and special laboratories for gynecology can be established within the department. It

pitals. In certain American schools, where obstetrics and gynecology are given in a number of different hospitals, it is deemed advisable to have separate chairs; since the physical plants are geographically so far apart, their correlation is a difficult task for one individual to control. In such instances, it is desirable that the instructor in obstetrics be well grounded in gynecology and the teacher of gynecology in obstetrics. While a physician may limit his instruction and practice to one or the other branch of the specialty, his efficiency will be all the greater if his fundamental training has been equal in both. An obstetrician who has not had thorough training in gynecology is handicapped in presenting the art to his students, just as a gynecologist who does not have a basic understanding of obstetrics is at a disadvantage in attempting to impart knowledge in relation to pregnancy and childbirth. If, for one reason or another, the head of the department prefers to teach obstetrics or gynecology, the other branch should be presented by an associate who may also hold a full professorship or who may occupy a prominent position in the department. If gynecology is not given the place which it deserves in a woman's clinic, it is likely to be appropriated by the Department of Surgery. Adequate preparation for the teaching of diseases of women involves a knowledge of pathology, bacteriology, endocrinology, irradiation, conservative treatment and surgical technic; obviously a long period of postgraduate study is essential to acquire this erudition. In the Tufts Medical School, although the chairs are separate, both departmental heads are in charge of unified clinics and practice both branches of the specialty.

In the past, one of the greatest hindrances to a combined department has been a well-planned course in obstetrics with very little attention being paid to gynecology. As pointed out, the practice of this art includes considerably more than the performance of an hysterectomy. The attitude of many teachers has changed materially during the last decade, directing their instruction toward diagnosis, office treatment, and the indications for operation. The technic of major pelvic operations should be left for postgraduate study and whatever time the undergraduate student spends in the operating room should be devoted to the study of living pathology. In other words, the time of the medical student should be utilized for basic sciences and whatever knowledge he can best acquire during his undergraduate days, rather than to subject matter which can be better obtained by postgraduate instruction.

That gynecology is not synonymous with pelvic surgery is manifested by the fact that only a limited number of patients with pelvic symptoms in a large clinic come to operation. At the New England Medical Center, a part of which is the Boston Dispensary, founded in

The American Board for Medical Specialties was organized in 1933 and 1934 for the purpose of coordinating graduate education and certification of medical specialties in the United States and Canada. This board reports to and functions in conjunction with the Council on Medical Education and Hospitals of the American Medical Association. It is made up of representatives from the Association of American Medical Colleges, the American Hospital Association, the Federation of State Medical Boards of the U. S. A., the National Board of Medical Examiners and the several special examining boards. This is evidence of the effort which the profession in America is making to elevate the standards for the various specialties. The effect of such constructive activity should be far reaching.

In order to ascertain the existing conditions in regard to the teaching of gynecology in North America, a personal study was started in October, 1934, and the list of medical schools approved by the Council on Medical Education and Hospitals of the American Medical Association, published in the *Journal of the American Medical Association*, Aug. 26, 1933, was used as a basis. There were listed 87 approved schools, 11 of which covered only the first two years of instruction, leaving 76 schools, 67 in the United States and 9 in Canada, which gave courses in gynecology. A questionnaire containing 17 questions was sent to the 76 professors of gynecology or professors of obstetrics and gynecology. Fifty-six, or 73 per cent, of these questionnaires were returned. The data compiled therefrom are, therefore, only approximate, but a sufficient number of schools answered to make the figures fairly representative of a cross-section of the departments in the United States and Canada.

It was found that gynecology existed as a separate department in 21 schools; that it was combined with obstetrics in 34 schools, and associated with general surgery in only 3 schools. In one instance in which gynecology is combined with general surgery, it is so allied only clinically; i.e., gynecologic patients are assigned to the surgical service, but the course in gynecology is separate and not integrated with obstetrics. In another instance, gynecology is combined with both obstetrics and surgery. Since the teaching is done in a university hospital, the patients are divided into two groups: (1) surgery and gynecology, (2) obstetrics and gynecology. The services are for three-month periods, the first three months the surgical and gynecologic service taking the tumor and inflammation cases and the obstetric and gynecologic service taking the plastic repairs and the functional cases. The second three months the order is reversed, etc. In the third instance gynecology is a division of the surgical department and is not combined with obstetrics. To summarize (Chart 1), gynecology is combined with obstetrics in 60 per cent, it is a separate department in 37 per

should be apparent that the physician who regards himself as a specialist should have a basic knowledge of the pathology involved in the lesions which he is treating conservatively or operatively, and that he should have at hand the proper facilities to impart this knowledge to his students. The formation of these services in gynecology or in obstetrics and gynecology offers another advantage and that is a place where the student may be further trained after leaving the medical school. Such services can be adjusted to offer two types of education: training in gynecology for a number of months as part of a general hospital internship and a residency where every few years a well-trained specialist may be graduated. The facilities for special training for men who have served long internships and desire to specialize in this branch of medicine are extremely limited in America. The establishment of gynecologic or of women's clinics in all large hospitals would be a logical solution of this problem. Working along these lines, the American Board of Obstetrics and Gynecology, in the April, 1936, number of the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*, published a survey of obstetric and gynecologic opportunities in 89 hospitals in the United States and 12 in Canada, this survey having been made in 1935.

H. J. Stander, in an article entitled "Teaching of Obstetrics and Gynecology in the United States,"* gives the following excellent reasons why the department of obstetrics and gynecology should be a combined one:

1. Both branches of the specialty deal with the physiology of the reproductive system of women.
2. We are just on the threshold of discoveries in such fundamental questions as the hormones, related to menstruation and reproduction; how can one not schooled in all phases of female physiology hope to comprehend, much less add to, the information of the intricate relationships of these hormones?
3. All progress in medicine depends upon careful observation and investigative work. Obstetrics and gynecology are in a field with common interests and its investigative work should be conducted in a combined department.
4. Operative obstetrics to be done well should be done by one familiar with and trained in operative methods and asepsis. Similarly the gynecologist, if he is to be somewhat more than a knife-loving operator, must have an obstetric point of view.

With this obstetric point of view in mind, the pelvic surgeon will refrain from doing high amputation of the cervix when treating cervical lacerations in young women during the childbearing age, he will not do abdominal fixation of the uterus in an attempt to correct retroversion or prolapse in women who are to have more children, and he will not remove the uterus to control hemorrhages of endocrine origin in the adolescent. I have previously emphasized, by figures, that the therapy of gynecology is mainly conservative.

*Am. J. Surg. 28: 67, 1935.

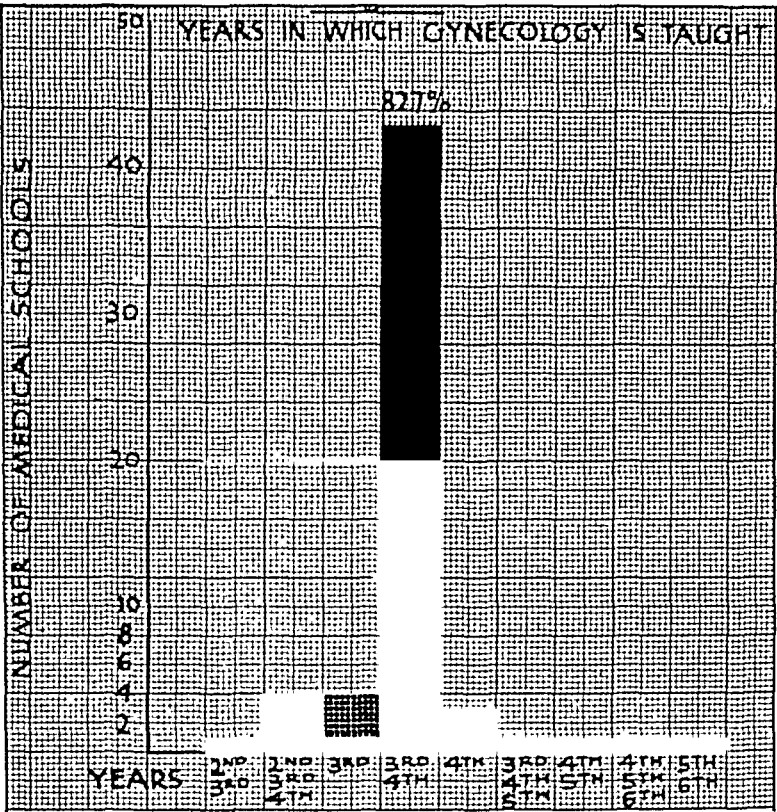


Chart 3.

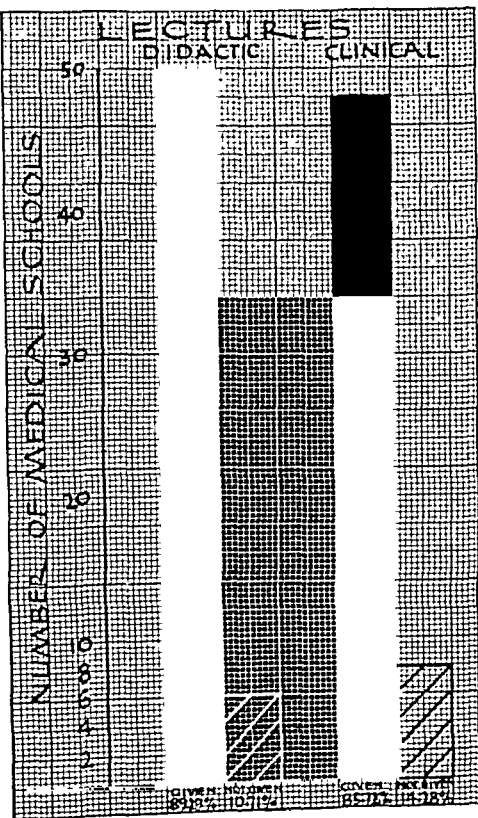


Chart 4.

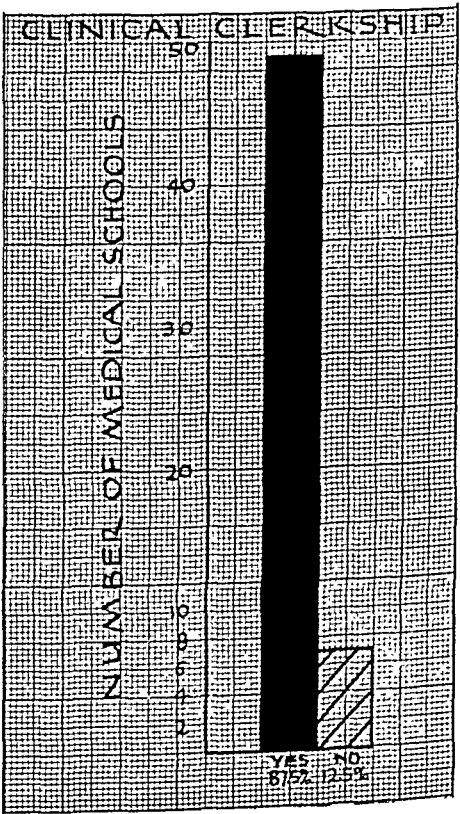


Chart 5.

cent, and it is united with surgery in 5 per cent of the 56 schools answering the question. The fact that the majority have a combined department tends to show that the ideal arrangement is being gradually reached, and further tends to imply that the small minority who still combine gynecology with general surgery should take steps to remedy this condition, if we correctly assume that the large majority are desirous of expending their efforts in the proper direction.

It was definitely shown (Chart 2) that gynecology is taught largely by clinicians and not by full-time teachers in these 56 schools, 39 schools having part-time, 12 schools both full- and part-time and 5 schools full-time teachers.

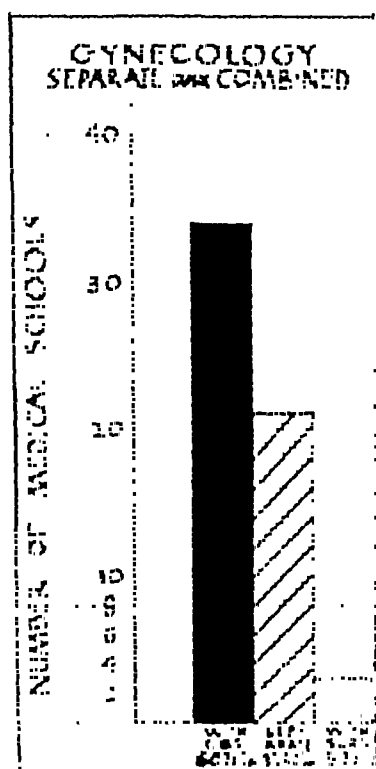


Chart 1.

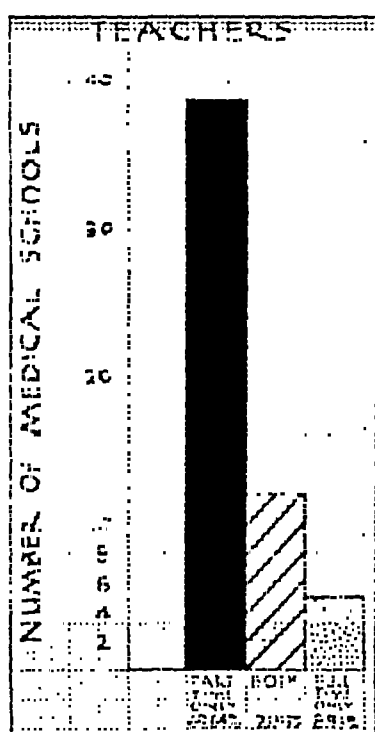


Chart 2.

Gynecology is taught (Chart 3) in the third and fourth years in 83 per cent of the schools in the United States which answered the question. The Canadian schools, because of their five- and six-year courses, teach this subject in the last two or three years. Didactic lectures (Chart 4) are given in 90 per cent and omitted in 10 per cent of these schools, while clinical lectures are held in 86 per cent, and not employed in 14 per cent, the figures being nearly the same. Didactic lectures vary from 6 to 72, the average number being 29, and clinical lectures from 4 to 224 with an average of 41, the highest number of lectures applying to obstetrics and gynecology being in a combined department. The subject was required of all students, and all stated that they were assigned to the out-patient department. This seems to

tion of patients in the out-patient department and the carrying out of office procedures in the treatment. Those who favor operative clinics do so in order to demonstrate gross pathology on the living rather than to inculcate lessons in technic. One of the best arrangements which is functioning at the present time in a combined department is the following: Third year, (a) didactic course and clinical lectures, (b) two months of gynecologic pathology and gynecologic ward rounds. Fourth year, (a) clinical lectures thirty-two hours; (b) two months' residence in the woman's clinic, full time, of which approximately one-third is given to gynecology, operating room, ward work and out-patient department.

To the inquiry: "Give suggestions you may have with regard to the teaching of gynecology, such as its place in the curriculum, methods of teaching, course, content, etc.," interesting and illuminating data were received. Space permits quoting only a few of the replies.

One professor of gynecology writes: "Obstetrics and gynecology should occupy a place in the curriculum equal to that assigned to general surgery. The course in gynecology should be interrelated with that in obstetrics. I favor a lecture course, ward work, out-patient department work, etc., carried out in a combined manner in these two."

2. Another answer: "I believe that gynecology is of less importance for the student than obstetrics. Emphasis should be placed upon pathology, diagnosis, and the method of treatment which is indicated. Do not believe that any attempt should be made to teach operative gynecology per se to undergraduates."

3. "Because of the great advances made in recent years in medical and surgical gynecology, this subject should by all means be taught as a major branch."

4. "I believe that didactic teaching during the junior year, with not too much emphasis on treatment and clinical teaching, with emphasis on diagnosis and treatment in the senior year, is a desirable arrangement, remembering always that gynecology is today to a large degree a specialty and should, therefore, not be overemphasized at the expense of obstetrics."

5. "Present set-up is a result of reorganization about four years ago. Up to that time gynecology had been a short didactic course, submerged in general surgery. It was taken out of this department and separate wards set up for it, which change has very much added to its importance in the minds of students and a very decided increase and general interest in the field."

6. "I believe the teaching of gynecology must vary in different schools with the clinical facilities and the personnel of the teachers in the department. We try to get away from the didactic recitation as far as possible, and substitute for it what we call studies in gynecology, in which we rely a great deal on visual instruction. Lantern slides are used and a notebook is used which is very profusely illustrated."

7. "I feel that the ideal is a combined department in a University hospital. In our own school we have separate departments for the reason that gynecology is taught in four hospitals and obstetrics in ten. It is practically a physical impossibility for one man to correlate this amount of teaching. I feel, because of this fact, better results are obtained by having separate chairs, although there is some overlapping in the clinical teaching in hospitals. Even though the chairs are separate, there is close cooperation between the departments of obstetrics and gynecology. The head of the department of gynecology has a combined obstetric

stress the fact that the teachers of this specialty in the United States and Canada are impressed by the value of out-patient teaching, which emphasizes history-taking, diagnosis, and conservative treatment.

As to the period of assignment to the out-patient department, 47 of the 56 medical schools answering showed a variation of three hours to twelve weeks with an average of twenty-two days or forty-four hours, assuming that two hours in the out-patient department constituted a day and six such days a week. In 87 per cent of these schools, students were assigned to the gynecology department of the hospital as clinical clerks (Chart 5), their term of residence varying from two to forty weeks with an average of nearly six weeks.

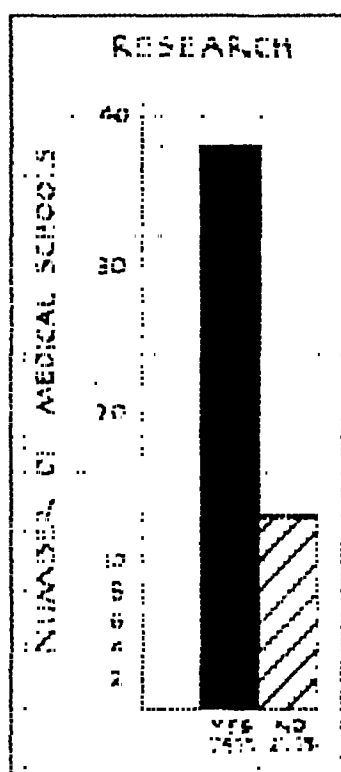


Chart 6.

Research (Chart 6) is carried on in the department of gynecology in 38 schools, or nearly 75 per cent, of the 51 schools which answered the question. In one of these schools research is an elective subject.

In answer to the question: "State your views with regard to a separate department of gynecology or a combined department of obstetrics and gynecology," 38 schools, or 68 per cent, favor a combined department, 14 schools a separate department, 3 schools have varied opinions and 1 school did not reply.

The answers to the question: "What constitutes an adequate teaching department in gynecology?" demonstrate that the large majority favor didactic lectures, limited in number, to give an idea of the scope of gynecology and to place emphasis on history-taking, the examina-

best care, the department of gynecology in large hospitals should be separated from general surgery and should function as a unit or as a part of a woman's clinic. Since only three out of fifty-six medical schools in North America combine gynecology with general surgery, the facts seem to be against such an alliance. Most teachers of gynecology express the opinion that the undergraduate student should spend most of his time in the out-patient department where emphasis is placed on history-taking, diagnosis, and office treatment. Pelvic surgery should be taught as a postgraduate subject, and the technic of operations should find but little place in the undergraduate curriculum. There is an increasing demand for well-established gynecologic or combined services in the large hospitals of America in order adequately to instruct the undergraduate student and to furnish residencies for those who desire to specialize in this field. The American Board of Obstetrics and Gynecology, sponsored by this Association, is playing an important rôle in the improvement of the practice of our specialty in this country. Relying on the progress which has already been made, the future may be faced with optimism.

GENERALLERGY AND METRALLERGY

J. R. GOODALL, M.D., AND R. M. H. POWER, M.D., MONTREAL, QUE.

(From the Wards and Research Laboratory of St. Mary's Hospital)

THESE two new composite terms are used to denote allergy of the genital system generally, and of the uterus in particular. Their derivation (from the old Greek verb, *γενω*, or from the more recent *γίγνομαι*, *γενήσομαι*, to bring into or beget; and *μήτρα*, womb, in combination with *ἄλλος*, other, altered, *ἐργον*, reactivity) signifies an altered or different reactivity of tissues of endowed individuals to substances that do not affect ordinary normals.

The substances that evoke these altered reactions are allergens, and the substances which they generate in the affected cells are allergins. These are poured out to neutralize the allergens when the latter come into contact with the specific sensitized cells. Allergens are widely distributed throughout the material world, and may be gaseous, liquid, or solid in character. They reach the innermost recesses of the individual, by absorption from mucous membranes, or by mere contact. Cells that resent the presence of allergens, develop allergins in their substance and thereby become sensitized to that specific allergen, and when this specific allergen is absorbed in quantities larger than the allergins of the blood stream can immediately neutralize, the excess

and gynecological hospital service, although he teaches only gynecology. I believe the teacher of gynecology should do a certain amount of obstetrics in order to have the obstetric point of view."

8. "Separate department develops better gynecologists. Better gynecologists deliver better gynecologic service to patients and better instruction to students. I believe the greatest contributors to gynecology have been men who do little or no obstetrics."

9. "I think that more emphasis should be placed on gynecologic pathology, both gross and microscopic. Inasmuch as gynecology comprises about one-half of the ordinary doctor's practice, my opinion is that more time should be allotted to this study than is given to it in the average school."

10. "Because of the fact that the general practitioner is frequently confronted with the problem of interpreting pelvic symptoms, gynecology should occupy a prominent place in the students' curriculum. In the teaching of gynecology, emphasis should be laid upon pathology, diagnosis, and the principles of treatment, and a discussion of the technic of operations should be limited to only the standard procedures. As to the method of teaching, didactic lectures covering the main subjects are necessary, but they should be supplemented by clinical conferences with exhibition of cases, discussion of case histories and demonstration of gross and microscopic pathology. Quizzes are undoubtedly of value not only in forming some estimate of what the student is obtaining from the course, but also to clarify the subject in the student's mind. I would prefer smaller classes as this would permit more personal instruction to be given to a smaller group of students."

11. "We see no reason for changing our system, although I believe the best teaching is in the out-patient department and not in the operating theater. The methods of diagnosis, pathologic demonstrations, and simple methods of therapy are all important."

12. "I believe in a preliminary didactic and demonstration course followed by clinical study with emphasis in methods of examination and diagnosis. Anatomy, physiology, and pathology are the foundation."

SUMMARY

There is at the present time a strong tendency in North America to unite the departments of obstetrics and gynecology into a combined department or woman's clinic. This unification offers many obvious advantages, since, in the study, the teaching and the practice of these two branches of medicine, overlapping constantly occurs. The physiology of menstruation and of reproduction, the interrelationship of the various hormones, which we are beginning to understand, are all factors which point to the ideal of a combined department. While the woman's clinic may function satisfactorily under one departmental head in the university hospital, separate chairs of obstetrics and gynecology are administered with greater facility in those schools in which these subjects are taught in several hospitals, as the coordination of the teaching where the physical plants are distantly apart is a difficult task for one individual to assume. However this may be, the teacher of obstetrics should have fundamental training in gynecology as the teacher of gynecology should have in obstetrics, if the best results are to be obtained. For purposes of teaching and giving the patient the

chronics, and there are those who are periodically allergic. These constitute the vast majority, and are chiefly those whose cases have been misunderstood because they are more difficult to detect.

In all the allergies there is a subsoil of hereditary susceptibility which may be exposed at all times as in chronic cases, or may crop up to the surface only when the oversoil is removed. The surface soil may vary in thickness, not only in families, but also in different members of the same family.

The symptomatic expression of allergy may also vary in the same individual at different ages. The allergy may shift its chief attack from one system to another, under the influence of age and environment, using that term in its broadest sense. Males with an hereditary subsoil are much more likely to show symptoms in the years of childhood, but females greatly outnumber them after the age of puberty, thereby showing the great influence exercised by endocrine imbalances upon the allergic substratum. This is important to grasp fully, otherwise endocrinology and allergy become inextricably interwoven in our appreciation of a patient's symptomatology. It is important to remember, that in such cases the endocrinologic imbalance is the adventitious or intermediate cause, but the allergic hypersensitivity is the constant factor always present, every ready to manifest itself when the general balance is upset.

In order to bring the matter more intimately home to our readers, we would like to broaden the subject at times, occasionally referring to some unusual, unrecognized, expressions of allergy in women, as regards their systems other than the genitals, because these digressions help to throw a great deal of light upon the more recondite manifestations of the same disease in the pelvic organs.

We have found so far, that allergy, of whatever origin, manifests itself in the pelvic system in the following symptoms, signs and pathology:

1. General pelvic edema and free fluid in pelvic cavity
2. Chronic endometrial edema and hyperplasia
3. Acute endometrial edema associated with the phases of the menstrual cycle
4. Menorrhagia
5. Acute menorrhagia
6. Metrorrhagia
7. Dysmenorrhea
8. Leucorrhea
9. Allergic vaginitis and vulvitis.

We wish to emphasize the fact that allergy is a general disease. It is due to a foreign substance in the blood, to which allergic hypersensitive individuals show a definite systemic tissue resentment, expressed in extravasation, and above all, a fact emphasized by all authorities on allergy, no system is immune to its influence.

allergen comes into contact with the sensitized cells, and an allergin is secreted which, by its irritating influence, causes local irritation and extravasation of plasma, by altering the normal function of the capillary lining, causing it to become excessively permeable to either plasma alone, or to all the components of the blood.

Allergins are the defensive mechanism of a highly sensitive person, much in the same way as many terrestrial animals and fish emit a defensive substance when danger is at hand.

The knowledge of the effect of the allergens upon the organs of generation is new. So little is at present known about it, that this study, we hope, will evoke a new interest. For us it has cleared many knotty problems. Pelvic allergy is full of interest and its victims are as numerous as those affected with the more easily recognizable forms of allergy. When the symptoms and pathology are described, it will doubtless create the surprise that it was not thought of before. For a better understanding of the subsequent description of pelvic affections of this nature, a short retrospect of the obvious manifestations will be of considerable help. Allergy expresses itself in one of two general ways. First, as an extravasatory disease, a protective reaction of which the common example is, of course, hay fever; and second, as an irritant to involuntary muscle causing spasm, of which again the classical example is asthma. There are many other diseases that are caused by one or the other of these two forms of expression, the commonest being antrum disease, migraine, urticaria, eczema, intertrigo, prurigo, local and general edema, angioneurotic edema, and neurasthenia. In this incomplete list omissions are conspicuous, but we have enumerated only the more obvious symptomatic developments.

One of the chief reasons that so little is known about allergy, is to be found in the fact that pathologists see nothing of it. Its chief manifestations are edema or spasm, both of which are not discernible at autopsy as a pathologic study.

But we feel that it is only a matter of time before a technic is evolved that will demonstrate the vascular changes which bring about the pathologic hyperpermeability, and the changes locally in the neuromuscular combination which cause continuous spasm under the influence of the allergins. Is the pathology primarily centered in the capillaries and the musculoneural endings, or is it a disease of the autonomic nervous system that brings about these changes in the affected tissues? There has been some thought spent upon these two theories, but it will probably be a long time before it is fully determined which is primary and which is secondary. Allergies are numerous, constituting from 28 to 60 per cent of individuals. There are those in this computation who are continually allergic, and constitute

greatly hypertrophied, but there was no pregnancy. Instead, the uterine mucosa was from an inch thick at the fundus to lesser degrees toward the internal os (Fig. 1). It resembled, in color, the pulp of a grapefruit, and was thrown into folds or convolutions like the brain, a picture, in every detail, resembling the edematous nasal and antral mucosa, under the changes characteristic of hay fever (Fig. 2). The true nature of this condition suddenly dawned on us, and in retrospect the whole of the past cases fell in a clear perspective.

The retrospect of her history in the light of this knowledge now became interesting. She has a markedly allergic family history, of asthma, bronchitis and eczema,

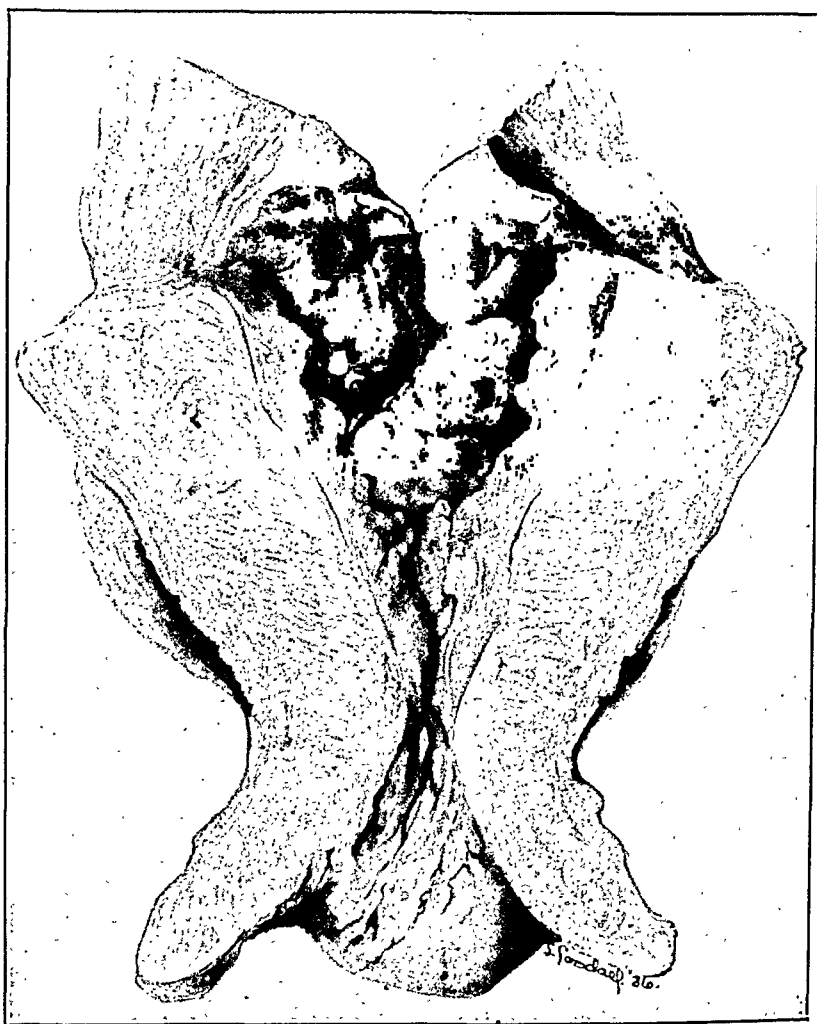


Fig. 1.—Showing swollen, bulbous mucosa and hypertrophy of muscularis.

and one of her three children is allergic to egg albumen. She had frequent nosebleeds as a child, that caused her parents great alarm, and so severe on two occasions as to cause the family physician to remain all night. These nosebleeds ceased when menstruation came on, and had not recurred since. She had retroplacental hemorrhage with one child and bled extremely profusely at that, and her other deliveries, twice to the degree as to cause great alarm for her life. In a very smooth recovery on the fifth day after the operation detailed above, she was pulling up the sheet so as to smooth it out, when she barely touched her nose. Epistaxis set in, and it was so profuse that she had to have her nostrils plugged. This ceased, and three days later she developed vaginal bleeding, at first slight, later

In 1914, Osler, when considering the subjects of purpura, asthma, edema of the glottis, hay fever and similar diseases, wrote "some day some anaphylactic key will unlock the door to this dark chamber." How true his prophecy! Only nowadays we use the term anaphylaxis for animals, and allergy for human beings. It is but a refinement of terminology, though there are certain distinct differences in the two diseases, due to differences in aeons of evolution.

For several years, Goodall was tremendously impressed when opening the abdomen, to find a diffuse edema of all the pelvic organs, a thickening of the peritoneum, and free fluid in the pelvic cavity. Many such cases have since been noted. The peritoneum is edematous, there are bullae upon the surface of the uterus, and widely dilated lymph spaces in the broad ligament; thickening of the bladder, toneless, edematous, swollen pale tubes; enlarged cysts of Morgagni and large edematous ovaries, sometimes without evidences of recent ovulation cycles, sometimes simple cystic hypersecretions. The uterus is larger than normal, and extremely soft, like an early pregnancy. Eight such cases were described before their true nature was detected. Let us describe one of these very pronounced recent cases in Dr. Goodall's service. Of course, it must be well understood that the signs described above, vary in degree in different individuals. At one extreme is the case about to be described, at the other extreme the signs may fade imperceptibly into the normal, and minor degrees of the condition might readily pass undetected.

The patient, Mrs. J., came complaining of menorrhagia. Her periods had always been prolonged, lasting, for two years after puberty, for seven days, and in the past two years lasting eleven days, during which time she was confined to bed, for the major part. The quantity was always copious. She had a constant watery leucorrhoea in the interval. She is a very intelligent woman, with an extraordinarily clear marbled skin, and abnormally pale-blue sclerotics. Something of the Lorrain type, without necessarily being "petite." She had a fairly marked cystocele and rectocele and a lack of tone of all the tissues. This is emphasized, because we think it an expression of overrefinement. It is a singular fact, that numerous computations among school children have shown that allergic children, or children of allergic parents, have a mental capacity far beyond their classmates. Her uterus was larger than normal, but symmetrical. Operation of repair and hysterectomy was advised. She was transfused and a wheal developed at the site of the puncture. No other untoward symptoms. The patient bled profusely during the repair, and when the abdomen was opened, there was a general edema of the pelvic organs, free fluid, etc., just as described above, and to Dr. Goodall's surprise, the uterus had all the characteristics of a two and one-half to three months' pregnancy. There was not the slightest doubt in his mind and in that of his assistant, that they were dealing with a pregnancy, though the patient had menstruated regularly, the last period being ten days previous to the operation. Owing to her past history, which will be detailed below, it was decided to do a total hysterectomy. When this was completed, the uterus was opened. The muscularis was like that of a pregnancy,

Knowing that cases of allergy are largely hypothyroids, and are frequently deficient in gastric HCl, these tests were made, and it was found that her basal rate was -15, and she was achlorhydric before and after a test meal. Her white cells showed a distinct shift to the right in a lympho- and monocytosis, all of which are frequent concomitants of, or causative agents in, allergy.

In the acute cases of pelvic allergy, the uterine mucosa alone may be involved, or the other uterine tissues to a lesser degree (Fig. 2). The major expression of the edema is always near the surface of the mucosa; the deeper tissues are more compact. In many instances one part of the mucosa is edematous, while another part is hemorrhagic. The mucosa is greatly thickened and may be associated with cyclic phases of menstruation. In many of these instances the condition of the cervix may give one a clue to the nature of the disease of the mucosa by a diffuse edema of the cervix, in which circumstances the cervix is swollen, usually one lip more than the other, semitransparent and boggy, signs characteristic of an advanced edema. Such cervixes, if cauterized, do not heal kindly.

Many of these patients, like others similarly afflicted, only in systems other than the pelvis, are allergic only at the menstrual period. This is where the endocrine imbalance and allergy become associated. It is a well-known fact that most allergies are worse at the menstrual periods, and the tremendous increase of allergic cases in females, at and after puberty, only substantiates this association.

Allergies are notably hypothyroid and hypoovarian and the natural inference is that they sink a little lower in their endocrine imbalance at menstruation, and the constant subsoil of hereditary allergic hypersensitivity comes to the surface. Menstruation does cause an increased thyroid and ovarian demand, and if these cannot be responded to, the general tissue well-being is correspondingly lowered. In these instances of sporadic allergy, it is not necessary to treat the allergy; it is only necessary to submerge it by thickening the surface soil, by administration of thyroid, and if need be, ovarian opotherapy.

Chronic menorrhagia and metrorrhagia are frequently of allergic origin. Many of these cases have come under observation. The difference between the plasma extravasatory types and the hemorrhagic types is one of degree, rather than of difference. However, one finds three types which may fade imperceptibly one into the other. The first is the extreme plasma exudative type as described at some length above. The second is one which shows less edema and more diapedetic extravasation; and the third shows no edema, but a thin atrophic mucosa with a bright red extravasated surface. The differences parallel similar allergic states elsewhere in the body.

more copious, until her condition became critical. There was no fever, and no infection. She was taken to the operating room, the clots were removed, and the vagina packed gently, and the patient was again transfused. She again developed a wheal at the site of puncture. Her recovery was uninterrupted afterward. The drawing made immediately after operation will clearly illustrate hypertrophy (Fig. 1). Microscopically, there was great thickness of the mucosa, and a diffuse edema, so marked as to separate the connective tissue cells as if by artefact. But it is not of this nature, because it is universal, involving the whole thickness of the uterus, but

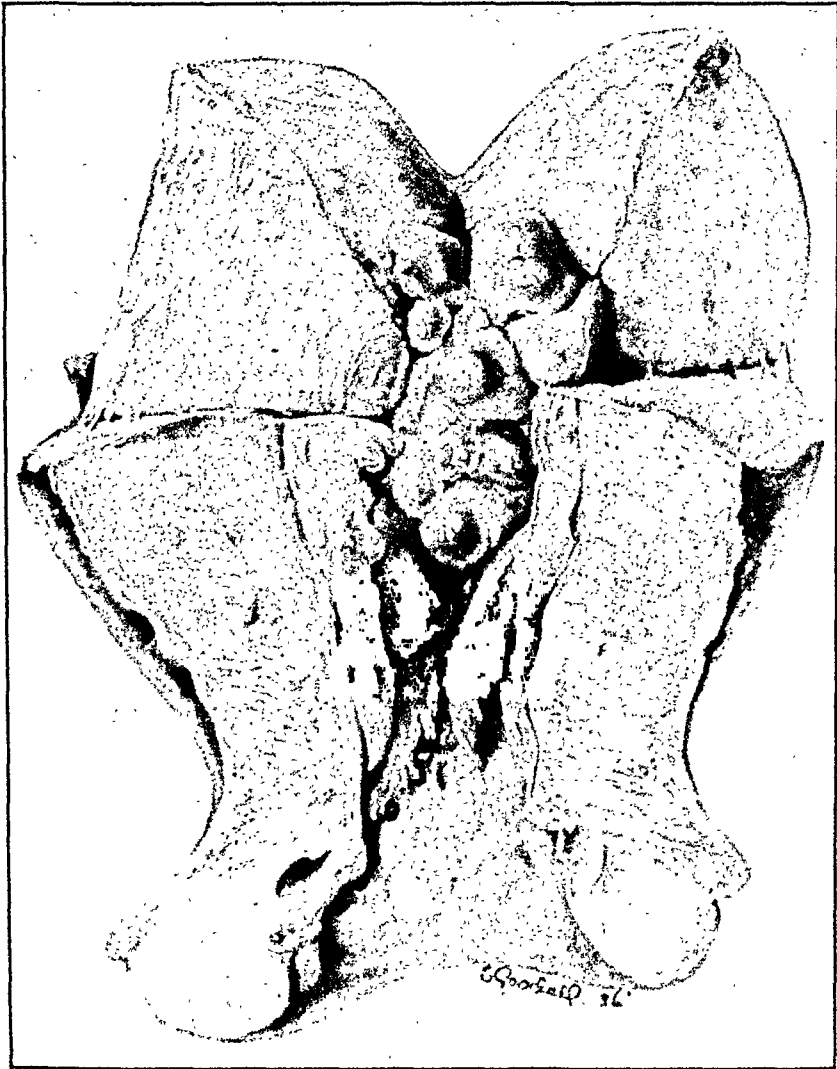


Fig. 2.—Mucosa and muscularis involved as in Fig. 1. The edematous mucosa hangs as a veil at the internal os. Cervix hypertrophied and edematous.

decidedly more pronounced near the surface layers of the mucosa. The microscopic drawings beautifully show the different degrees in the various depths of the mucosal tissues.

There was in this case, owing to the chronic irritation occasioned by the allergin and the consequent extravasation of plasma, a chronic hypertrophy of all the tissues of the uterus and a hyperplasia added to the great thickness occasioned by the edema. The microscopic picture is strikingly like that of the antrum of Highmore under similar causal agents.

acterized by laborlike pains, but usually more continuous during the first hours or day of the flow. It has nothing characteristic to distinguish it from the ordinary type of dysmenorrhea in young girls. But it should be suspected in such cases, and an inquiry made into the family history for evidence of stigmas of allergy. One has always a means at hand to prove the etiology. By injecting from two to five minims of 1-1,000 solution of adrenaline, the case reacts promptly if of allergic origin. Unfortunately, the relief is only temporary, but the injection may be repeated in small doses. Another and very old-fashioned remedy, the true significance of which was perhaps never suspected, consists in giving a large dose of castor oil two or three days before the expected period, and then recommending that the patient remain on a milk, or greatly reduced diet, until menstruation is over, or at least well established. If in such cases the allergy was of alimentary origin, and the offending substance was eliminated, the patient was greatly improved. If the allergy was not of alimentary origin, or of some dietetic substance still included in the reduced dietary, then improvement did not follow. The usual explanation of the frequent improvement brought about by this treatment, was that it decongested, and was antiphlogistic.

Let us illustrate a few cases. A young girl, free from dysmenorrhea except periodically, and that rarely, went to work in a flower shop. From that time on her dysmenorrhea was severe and incapacitating. The relationship of this occupational cause to the sudden onset of the symptom having been established, she relinquished her position for another type of work, and was completely relieved.

Another patient suffered excruciatingly with menstrual dysmenorrhea. This symptom had come on after a rather severe infection in the nature of a crop of boils, which left her anemic and fatigued. Large doses of ammonium citrate of iron gave almost magical freedom from dysmenorrhea. Cases of this nature are very numerous.

A young girl of our circle of acquaintance developed severe dysmenorrhea after an operation for an acute appendicitis. The dysmenorrhea was always associated with bowel tenesmus and upset stomach. Previous to her appendicitis she was unconscious of any discomfort at menstruation. Later she developed a severe nasal infection and became definitely and periodically asthmatic. Her basal rate was found to be -12. When placed upon thyroid and iron tonics, her general condition improved and her dysmenorrhea and asthma became completely covered, after having been discovered for a period of about nine months.

Another case is of more than passing interest. The patient is so incapacitated by her menstrual dysmenorrhea that she will not go from home at that period, for fear of disturbing her entourage. She has been in the hands of many prominent gynecologists of this city, and treatment by Goodall proved equally futile. The girl was likely to become an alcoholic and morphine habitué, because she took gin in large quantities and morphine had to be exhibited several times to give relief, and stop her screams. She was given a hypo of adrenaline, and the relief was almost instantaneous, except for a residual pain following cramps. She is now under observation. Her thyroid is -22. She has no free hydrochloric acid. Her family

Let us outline one of the latter types. Goodall has had to revise his dicta upon the subject of hemorrhage in cases of that disease variously described as chronic metritis, chronic fibrosis uteri, and chronic subinvolution. This disease of the uterus usually precedes the onset of menorrhagia and metrorrhagia by many years. But suddenly we find these signs appearing without apparent reason. To arrest the hemorrhage, operative procedures or sterilizing methods have frequently to be resorted to, and Dr. William Fletcher Shaw once stated, "These procedures are expressions of defeat." There is, of course, a reason for the onset of hemorrhages, but in most cases of the chronic fibrosis and in many instances of fibroids, and in still more instances of total absence of local pathology, the cause is a general allergy. Many of these are spoken of as idiopathic, myopathic, and endocrine. The two first terms mean nothing. The latter may operate in a large number of cases, either alone or as an adjuvant, in exposing an allergic, heretofore dormant, predisposition.

Let us return to our case. Mrs. L., thirty-six years of age. Mother of three children. Has always had profuse menstruation. Three years ago developed metrorrhagia. Was treated in the radium institute with three series of deep x-ray of 14 sittings, 42 in all. This arrested menstruation for six months. Metrorrhagia set in again and she was subjected to 14 more sittings of 'deep x-ray, without any appreciable effect upon the blood loss. She then came to St. Mary's, a thin little woman, complaining of attacks of migraine and pain about the chest. There was a family history of allergy, and she had deprived herself of bread and all substances made of wheat for many months. On physical examination, the cervix was almost infantile, and the uterus was hyperinvolted, and hard. Total hysterectomy was performed after transfusion. The uterine mucosa was blood red everywhere, and atrophic. Five days after operation she had two nosebleeds, copious, followed by several others in the next few days. Neither this patient nor the previous one showed any epistaxis while on reduced diet. We later told her to eat some bread. She shortly afterward became chilly, with cold extremities, and a cold perspiration and a great acceleration of the heart rate, and precordial pain. These symptoms were reproduced at will by the ingestion of bread, and the attacks of epistaxis were more or less synchronous.

Many of the cases of pelvic allergy become so, only on occasions when the general health is lowered by menstruation, worry, fatigue, exhaustion, after periods of mental or physical stress, and after any infection. Most of these are interpreted in terms of the conditions enumerated, and treatment directed to the underlying cause is not necessary. Hence the actual cause is seldom detected, one sees only the intermediate. Many patients become allergic in one or another system after operation, a condition that is seldom recognized, and therefore seldom properly interpreted.

Allergic dysmenorrhea is a fairly common condition. It falls into the group of the muscular spasms. Allergic dysmenorrhea is char-

In other instances, other allergens are the cause. In one instance, the patient at menopause developed an allergic eczema of the auditory canal and suffered frightfully from intolerable itching. She later developed prurigo, and still later an insufferable vaginitis and eczema of the vulva. Her sugar content was normal. She was a -12 rate, no free hydrochloric acid, but a distinct eosinophilia. Reductions of her diet to boiled skimmed milk, and the exhibition of thyroid and hydrochloric acid, brought about a rapid amelioration of symptoms. Later it was found that she had become allergic to potatoes, and when these were excluded from her diet her continued enjoyment of life was restored.

May we digress here, to consider a few relevant cases of allergy in gynecology, and incidentally these remarks must apply to men, though perhaps less frequently, or in a mitigated form. In our wards at present is an elderly single woman who came in exhibiting great pallor, orthopnea, general anasarca, uterine hemorrhage, and severe dyspepsia and precordial pain. Headaches were severe. She had lost all the hair of the scalp and of the normally hirsute areas. She at once impressed one as being in the last steps of Bright's disease. However, on examination, the heart was negative, and the lungs showed some rhonchi and râles. The urine was absolutely normal, as was also the blood chemistry. There was an advanced degree of anemia. Her basal rate was minus 12. She was transfused and given iron. She improved rapidly. The edema and respiratory distress disappeared completely, and her headaches gradually were alleviated. We then undertook to do a hysterectomy for fibroids. She went through the operation perfectly and was remarkably well for five days, when she developed a left leg thrombosis and temperature. Almost at once she became allergic again, with inability to take food; precordial pain, return of the headaches and a feeling of weakness, and generally wretched. She improved promptly again under a 10 per cent glucose intravenous injection and twenty-four hours later, another blood transfusion. This case illustrates beautifully the double onset of allergy under first, a condition of lowered vitality, and later, after a post-operative infection. These cases are extremely numerous, and we are convinced, after a careful examination of the fibroids, that the uterine bleeding in this case was allergic, and did not proceed from the growths. The fibroids and their surfaces were almost unaffected, but the rest of the uterine mucosa was hemorrhagic and infiltrated with eosinophiles. Another patient just discharged from the wards of St. Mary's affords a clear vision of another common gynecologic association of allergy and colitis, with referred symptoms.

Mrs. L., an elderly lady of sixty-five years, but of much older appearance, came into the ward complaining of precordial pain, epigastric pain, cold, numb feet, and headache. But her chief complaint was pain in both lower quadrants. The pelvis was negative. X-ray of gallbladder and barium series were negative. The diagnosis of acute exacerbation of a chronic colitis was suspected from the first, later confirmed. It was also suspected that the precordial pain and headache and numbness of extremities were allergic. She improved tremendously under rest and treatment. But in a sudden bout of exaggerated colitis, she developed acute precordial pain, simulating angina, followed by a severe attack of allergic asthma. Her condition was most distressing. The house surgeon, Dr. Macphail, aware of our diagnosis, immediately gave her injection of adrenaline, with prompt relief.

history is replete with allergic roots, and hope is high that she will ultimately be cured by finding the allergen or allergens that are causing the cramps. Meanwhile she is on thyroid therapy, combined with dilute hydrochloric acid and pepsin.

Enough cases have been described to demonstrate the type and procedure adopted.

Leucorrhea of allergic origin is more difficult to establish convincingly. However, in a paper written two years ago by Dr. Goodall, which appears in the *Journal of Gynecology and Obstetrics of the British Empire* for October, 1936, 200 cases of mucous colitis are described, with all the symptoms arising out of referred pain in such cases. A very large percentage of spastic colon in mucous colitis are allergic in origin, and in that paper several nurses volunteered the information, that they had periodic attacks of leucorrhea and that these always synchronized with exacerbations of their colitic symptoms, and with improvement of the symptoms of colitis under rigid diet, the leucorrhea disappeared completely.

Another form of leucorrhea is met with in the next category of cases. Those of allergic vaginitis and intertriginous vulvitis. These patients complain most bitterly of pruritis vulvae, and irritating acid discharge. On examination, an extravasatory intertrigo is found about the vulva, in the cleft of the buttock, in the anal orifice, and in the folds of the inguinal area. The tissues in the more chronic cases, crack and expose the tender corium. Scratching often leads to infection and a complicating impetigo. In many instances, signs of kraurosis vulvae are already present. The vagina is reddened, pruritic and burning. It is edematous, the natural rugae are increased, the surfaces are desquamative, and the underlying surface looks raw and angry. In some cases, patients have of their own accord, inserted cotton in the vagina and vulva to separate the affected and contiguous surfaces. The family history is usually affirmative, and the patient may have had other signs of allergy in other parts of the body. Allergic vulvitis, due to glycosuria, falls into this category of allergic vulvitis and vaginitis. This condition is absolutely indistinguishable from the description given above. The popular idea among medical men that diabetic vulvitis and vaginitis is due to local decomposition of the glucose of the urine, is entirely wrong, for no matter how clean a woman, the symptoms persist, and some of the worst cases of diabetic vulvar allergy which we have seen have been in cases where sugar was never found in the urine, but a high blood sugar was present, the overflow into the urine being prevented by a high renal threshold. Reduction in the blood sugar content invariably leads to prompt relief. This is a vulvar allergy in which the allergen is glucose, which exists in such quantity in the blood that it sets up an allergin in the affected tissues.

administered, upon the assumption that it was a case of ptomaine. That afternoon her headache increased; she became stuporose, facial paresis and paresis of the upper extremities set in. By evening she was completely comatose, and propulsive vomiting, widespread paresis, and changes in the optic discs had developed, all indications of intracranial pressure. Doctors Goodall, Scriver and Cone, gynecologist, internist and neurologist respectively, concluded that this was a case of choroidal hemorrhage, probably associated with toxicity of pregnancy, on the assumption that all pregnant women are toxic, though there were no signs of toxicity or diabetes. Her spinal fluid was under high pressure but was free from blood. It was decided that it was advisable to interrupt the pregnancy. This was done by cesarean section. The case was very hemorrhagic at operation. She promptly improved, was lucid in twenty-four hours, and nonparetic in forty-eight. The inference was, of course, that the condition was due to the pregnancy. Its true significance did not develop until three months later, when after a meal of mackerel, she developed the same symptoms, paresis, vomiting, diplopia, and screaming headache. She was immediately taken into the hospital, given a gastric and colonic lavage and 3 minims of adrenaline. The symptoms subsided as if by magic, and recovery was complete. This was undoubtedly a case of allergy of the brain, not a choroidal hemorrhage, but a choroidal edema. Hence its rapid disappearance under treatment. Let us repeat, there is no system in the body that is exempt from the effects of allergins. It is intensely selective in its incidence, though not infrequently it is composite in the one individual by attacking two or more systems simultaneously, or in sequence.

One other case: A young woman had suffered a severe toxemia of pregnancy, complicated by numerous convulsions. The baby was lost in delivery, and the mother's puerperal recovery was slow and eventful. She was sent home in the ambulance, three weeks postpartum, when she promptly developed a most severe retrosternal pain, with a degree of temperature. Low grades of temperature are not uncommon in allergic patients. Goodall was called in consultation, and after examination, pulmonary infarct was suspected, but the picture did not fit the diagnosis. However, *faute de mieux*, it was maintained. Patient had several of these attacks, all similar, without any objective signs. She took very little food, vomited a great deal, felt that food made her worse, and brought on the attacks, so that by abstention she was reduced to a state of severe malnutrition. Suddenly something clicked (in the surgeon's brain, we mean). It is allergy. She was sent to another hospital, the basal metabolic rate was found to be -18, no free hydrochloric acid in the stomach, and a grave hypochromic anemia was detected. With her next spasm she was given 3 minims of adrenaline, with immediate results. She was then put on thyroid, with pepsin and hydrochloric acid, and her symptoms promptly subsided and her nutrition was quickly restored. But perhaps the greatest change was in her mental state. From a depressed, apathetic, hypochondriac, she soon recovered her pristine buoyancy and *joie de vivre*.

This is another instance of the importance of raising the general health to overcome a specific cause. To those who do a great deal of gynecologic surgery, the composite picture of pelvic allergy, complicated by pelvic inflammatory disease, will readily recur. Of course, one does not operate upon pelvic inflammatory disease nowadays except in occasional cases. When these two diseases co-exist, we find a diffuse inflammatory pelvis, over which large and small lakes of clear yellow subperitoneal or subadhesional lymph exist. The lymphatics of the pelvis are widely dilated, and many of them have a clear coagulum in them. The blood vessels of the broad ligaments are engorged, and

It has been our experience that many of the cases of weakness, fatigue, and lassitude which come periodically over women who, at other times, are inordinately filled with energy, are due to temporary allergic states brought about by exhaustion or other contributory factors. And sudden changes of disposition are attributable to similar causes. We feel certain that many who bear the stigma of neurasthenics fall into this category. In fact, it is well recognized that allergic individuals change their character completely when under the influence of an allergen.

Apropos this subject. Mrs. H. was in one of the hospitals of this city some four years ago, suffering from what was considered cardiac asthma. She was under the observation of some of the best cardiologists for a period of six weeks, without any appreciable improvement. She was then advised to go to Atlantic City, which she did, and promptly grew worse. She was brought back to Montreal in an ambulance, and it was thought futile to seek further treatment. However, uterine hemorrhage set in, Dr. Goodall was called. She had passed her menopause. Patient was sitting up in bed, grasping the sides to fix her chest. Her chest was overexpanded, she was markedly cyanosed. A most pitiful picture. Pelvis negative. However, examination of the abdomen revealed a huge colon, the size of my upper arm. The bowels had been moving daily. Dr. Campbell P. Howard was called in consultation. Castor oil in large quantities was administered, and high colonic lavage instituted. The amount of fetid material that was brought away was incredible. The asthma was promptly relieved, and the patient has been able to play golf and drive her car without recurrence, for the last four years. Recently she began to slip again. She is now becoming so cranky and so neurasthenic that she is almost impossible of association. This is but another manifestation of her allergic state, the true nature of which it is impossible to determine, and being so chronic, would probably not respond to any form of treatment. Moreover, her advancing years makes rehabilitation more difficult, so that the outlook is poor. She is looked upon by all who contact her as one of the worst of neurasthenics, whereas she is but a poor allergic, with a very bad family tree rooting in a bad subsoil.

These cases deserve our most inquiring, unexpressed sympathy and study. Where in such cases the allergic sensitivity becomes active, owing to general ill-health and advancing years, the outlook is far from encouraging, and will tax our ingenuity to its limits. Most of us surgeons of experience find hours too filled to give these cases the study they require, and they end up with a loss of faith in the profession usually.

From a gynecologic and obstetric interest we cannot refrain from detailing two of the most interesting cases.

The first is a woman, thirty-four years of age, upon whom Dr. Goodall performed a cesarean section three times. She has a bad family history of allergic sensitivity, and she, herself, has suffered from migraine for years. Migraine, it is well known, is due to an allergic edema of the brain. She is allergic to certain kinds of fish, and one of her children is allergic to milk. When she was five months pregnant, she ate some shellfish at her evening meal, and shortly afterward, she had the "migrains." That night, vomiting set in, and the next morning castor oil was

views. Issue was taken, too, on many of the statements made in the paper. For example, Dr. Gay tells me that hypothyroidism is not at all characteristic of allergy, and that absence of free hydrochloric acid is likewise not significant. There were many other similar criticisms made, but I shall go into no further details with this second-hand criticism.

My own reaction to the paper is that the authors have not been sufficiently critical in their explanation of many of the interesting cases reported in the paper. Such a picture as that shown on the screen, of an enormously thickened, polypoid endometrium, would suggest an extreme type of polypoid hyperplasia. Indeed, Dr. Goodall includes hyperplasia among the possibly allergic diseases, a view totally at variance with what we know of its endocrine mechanism, and I do not believe he has made out a case. As a matter of fact, he suggests the hypothesis that in these cases there is a subsoil of allergy which may be covered over by an endocrine defect, but the evidence presented on this point strikes me as very unconvincing. For example, he stresses the frequency with which allergic phenomena are associated with endocrine defects and crises. On the other hand, I am told that in our allergy clinic in Baltimore more girls between the ages of six and ten suffer with allergic manifestations than do those around the age of puberty. Nor are weakness, lassitude, and general debility characteristic of allergic states.

The far-reaching conclusions of the authors of this paper are based on evidence which I do not believe will be considered adequate. This is not to say that allergy cannot be a causative factor in gynecologic disease or symptoms, for the evidence in at least a small number of reported cases, especially of dysmenorrhea, makes one feel that it may at times play a part in their production. But this is very different from accepting the view that allergy is responsible for the extensive pelvic changes pictured by Goodall, changes which are far more rationally explained by other causes.

DR. R. M. H. POWER, MONTREAL, CANADA.—There are just three salient points which I should like to emphasize: (1) *Hereditary allergic subsoil (permanent in each individual)*. Allergics constitute approximately 28 to 60 per cent of all individuals. Some are continuously allergic and constitute the chronic cases, while others are periodically allergic, hence the acute cases. In the allergies there is a definite subsoil of hereditary susceptibility. It may be exposed at all times as in chronic cases, or may crop up to the surface only when the oversoil is removed.

(2) *Individual surface soil which when removed by ill-health arising out of any cause may cause a subsoil exposure—then the patient becomes a "facultative allergic," until health is restored*. The surface soil may vary in thickness, not only in families but also in different members of the same family. It is also important to note that symptomatic expression of allergy may also vary in the same individual at different ages. The allergic influence may shift its chief attacks from one system to another under the influence of age and environment.

(3) *Permanent allergies are common cases of thyroid hypofunction and achlorhydries. Restoration of these functions by medication frequently relieves the allergic state*. Many chronic cases of allergy are hypothyroids. We have found the usual metabolic rate to be about minus twenty. They are also achlorhydries and are relieved by the administration of hydrochloric acid and thyroid medication.

DR. SMITH (closing).—About ten years ago when we first started this work, a prominent allergist in St. Louis told me that his patients had not complained of dysmenorrhea but that he had not inquired of their menstrual history particularly. Upon my suggestion he began to ask specific questions in regard to the menstruation of his patients, and he has now found that his patients were relieved of dysmenorrhea following appropriate treatment for other forms of allergy. I believe that a careful menstrual history over a period of years will definitely show that dysmenorrhea is a part of the picture of allergy.

adhesions, when broken through, are inordinately oozy. The lymph collections may vary in size from millet seeds to that of an egg. The uterus is large and soft, and not infrequently the outer third of its thickness is under a white coagulation of all its tissues. The ovaries are edematous and usually, though not constantly, filled with small cystic follicles in which the egg may or may not have surrendered.

We believe that many conditions at present not generally attributed to allergy are allergic basically, such as pseudoanginal attacks, precordial pain, many cases of colitis, acidosis, sudden death in children and adults without pathologic findings, for the conditions of edema and spasm, the chief expressions of allergy, are unrecognizable at autopsy, or are looked upon as postmortem fluid gravitation. The periodic overabsorption of unsplit proteins may depend upon many extraneous causes enumerated above, so that the normal neutralizers in the blood are used up and the excess of allergens evoke the allergins of sensitized cells, cardiac or other. We would include many instances of neurasthenia with headache radiating down the back of the neck. We think also that those cases of spasm of the common or cystic bile duct, simulating cholecystitis or gallstones, are of this nature, as are also the muscular spasms of pregnancy. It is intriguing also, to think that erythroblastosis in the infant may be hereditary from one or both parents, or due to placental transfusion from the mother. There is much to substantiate this. We would include from observation, many cases of lassitude and fatigue, and general feeling of malaise, frequently associated with general skin irritation after the day's work, such that clothes must be removed. These, we think, are temporary allergies due to prolonged effort, mental or physical, in which specific treatment, owing to its composite nature, is of little avail, but change of environment and surcease from mental bombardment and physical effort will recover the subsoil and restore equilibrium.

Treatment in the acute cases is often surprisingly gratifying, often a complete cure. In the chronic cases, it is often not even a mitigant. Nevertheless, the satisfaction to the physician and surgeon is the knowledge that he is dealing with a clinical entity. Unfortunately, it is an entity which, in most cases, is hidden from the pathologist.

1472 SHERBROOKE STREET

ABSTRACT OF DISCUSSION

DR. EMIL NOVAK, BALTIMORE, Md.—The ideal discussant for such a paper as this would be an expert allergist, for most clinicians, like myself, have only a very superficial knowledge of this still very confused subject. I have tried to do the next best thing by asking an expert in the subject, Dr. Leslie N. Gay, Chief of our Allergy Clinic, to read this paper and comment upon it. In general I may say that these comments were definitely unfavorable, and that the general views on allergy expressed in this paper and the evidence submitted as to the allergic basis for many of the reported cases were considered by Dr. Gay as not in conformity with accepted

intraabdominal weight should not be carried by a poorly developed composite sheet of muscle (the levator ani) evolved from the caudal musculature. In the erect posture, the symphysis pubis and its rami, with the arch bridged by the urogenital diaphragm, lie in a horizontal plane; these structures, therefore, bear the weight of intraabdominal contents transferred to them by reason of the human erect posture.

The urogenital diaphragm is a structure peculiar to man. It not only reduces the size of the anovaginal cleft but, by reinforcing as it does the so-called levator ani, its central free margin forms a conjoined tendon to which, on its inferior surface, is firmly attached the superficial perineal musculature, while the upward extension of this undifferentiated mesenchymal block of tissue as the "perinealkeil" forms the rectovaginal septum.

The superficial perineal musculature plays a most important rôle in maintaining the normal topography of the perineal parts. A permanently stretched or damaged sphincter vagina permits the perineal body, through the medium of the sphincter ani externus, to be drawn backward.

Between the levator ani with its fascial covering above and the urogenital diaphragm below, lies the wedge-shaped anteriorly directed diverticulum of the ischiorectal fossa packed with dense fat; the so-called pelvic diaphragm is thus supported throughout, directly and indirectly, by the urogenital diaphragm.

On the pelvic floor, and firmly attached to its walls, is cellular tissue in which are imbedded the pelvic viscera. In fetal life the pelvic basin is well filled with such fascia, the pelvic viscera at birth being relatively near the pelvic brim; as puberty approaches, this supporting tissue becomes materially compressed so that certain portions become condensed into so-called pelvic ligaments.

The arbitrary division of the pelvic cellular fascia known as the uterosacral ligaments is, however, essential in maintaining the vagina and uterus in their normal positions. The attachment to the sacrum is not constant, frequently being spread in a fan-shaped manner over the anterior portion of the sacrum, extending in some instances as high as the pelvic brim. The fibers converging are inserted into the uterus at the junction of the cervix with the lower uterine segment. The fascia is richly interspersed with smooth muscle; it receives the same innervations as the uterus; it follows the same physiologic variations, becoming hypertrophied during pregnancy and undergoing atrophy with recession of ovarian activity. These structures Luschka termed "musculus retractor uteri." Tandler⁹ maintained that owing to the constant tone of these ligaments the excursions of the uterus and

DR. JAMES R. GOODALL (closing).—Dr. Novak has quoted Gay, the allergist, in refutation of some of my statements. I would refer Dr. Novak, on the other hand, to the works of Bell of London, and Schumacher of Boston, men of international reputation, whose textbooks are found on the desks of every student of allergy. My statements in reference to the association of allergy and endocrinology are drawn from these sources.

As a further example of allergy, let me refer to the vulvar disease in glycemia, which most of us have been told is due to the local decomposition of the sugar in the urine. We have got to change all this teaching. Eczema of the vulva in glycemia is an expression of allergy, just as eczema under some conditions in other parts of the body is an expression of local irritation due to the sugar in the blood. The patient I have cited in my text was a diabetic with a high renal threshold, and none of the sugar escaped into the urine. Such cases may be multiplied. The present one suffices to indicate the trend of thought.

In further rebuttal of Dr. Novak's criticism, I may state that my remarks have been misunderstood. The condition of profuse pelvic inflammation covered by large lakes of lymph such as I have described in my text, is not produced by allergy alone, but by a combination of two diseases, an inflammatory infective process and an allergy, which complicates and aggravates the whole.

VAGINAL HYSTERECTOMY IN PROLAPSUS UTERI

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PROLAPSUS uteri may be regarded as a sacropubic hernia and as such the displacement of the uterus is but the visible sign of a general descent of all the pelvic viscera. As a result of such a disturbance in the topography, pathologic lesions of these and associated organs are frequently encountered. It must be further borne in mind that the symptoms of any hernia are rarely restricted to the actual contents of its sac but may be, and often are, far reaching.

While the causes (actual and contributing) of prolapsus uteri are divergent, the anatomic changes permitting the hernia are in the main similar; the frontispiece in W. S. Campbell's *Surgical Anatomy* is particularly applicable in the repair of genital prolapse, "Surgery is anatomy practically applied, and the anatomic mind is as essential to the surgeon as the aseptic conscience."

In most mammals, and particularly in those of the pronograde type, the weight of the abdominal viscera and the force of intraabdominal pressure are largely borne by the muscles of the anterior abdominal wall. In man, coincident with the adoption of the upright posture, the vertebral column has developed certain characteristic curves. Such curvatures not only absorb shock transmitted to the cranial contents and other viscera but, also, insure that the greater brunt of

Into the cellular tissue extends the lower end of the peritoneal cavity, as the culdesac of Douglas. The lower limit of the pouch is not the same in any two individuals; when extremely deep, the condition suggests a general deficiency in retroperitoneal cellular support.

Body cavities responding to variations in internal pressure are usually closed by striped muscle for equalizations of pressure.⁹ The musculature constituting the pelvic floor acts antagonistically to intra-abdominal pressure. While the innervation is different, both the abdominal and pelvic musculatures act synchronously and synergistically. When the muscles supporting the pelvic floor do not contract in response to pressure from above, descensus of the pelvic organs naturally results. Normally, the levator ani contracts in response to increased intraabdominal pressure. The tonus of the levator muscles is essential in preventing the pelvic organs from yielding to the normal downward thrust, yet, with straining, the resistance is overcome and as a result the perineal hiatus is enlarged.

FACTORS IN PROLAPSE

It is difficult to say with certainty the degree contributed by any one factor in the production of prolapse, and it would seem that only in rare instances can the condition be ascribed to a single cause.²⁰

Normally, the length of the mesentery of the small bowel prevents its descending into the true pelvis; if, on the other hand, the mesentery be unduly long, it becomes apparent that, should a deep culdesac be present, there exists in such an individual a potential uterosacral hernia. Vaginal relaxation permits such a hernia to become enlarged, ultimately carrying with it the vaginal canal, the uterus and, eventually, the bladder. The condition, therefore, may be rightly compared with the so-called sliding hernia of the cecum and sigmoid, in the right and left inguinal regions, respectively.

A contributing factor in the development of hernias is the toxic effect of infection upon the normal tone of both voluntary and involuntary muscles; the elasticity being thus impaired, these muscles yield readily to strain. Particularly is this true with the muscles supporting the pelvic viscera. Keys¹² suggests that even the exanthemas in the young predispose to prolapsus uteri. Urinary tract infection accompanies over 2 per cent of all pregnancies; a large percentage of such cases do not respond to the accepted methods of treatment. If even a moderate degree of sacculation of the base of the bladder be present, the condition becomes particularly refractory to treatment. Assuming the rôle played by focal or general infection on muscles, further relaxation developing with repeated pregnancies then becomes a vicious circle, as the toxic effect of recurrent and protracted infection causes loss of tone in the supporting musculature, which in turn

vagina are limited. Richet and Walcher (quoted by Halban and Tandler) regarded them as the most important structures in preventing prolapsus uteri.

Extending from the posterior aspect of the pubis, and firmly attached to the uterus on a slightly higher level than the uterosacral ligaments, is the pubocervical fascia on which the bladder is dependent for its support; though more condensed, it is not anatomically independent from the lateral portion of the cellular tissue. These two so-called ligamentous bands, the uterosacral and pubocervical fascia spanning the pelvis in an anteroposterior direction, must then in the normal individual be considered antagonistic in action, thereby maintaining²² the topography of the pelvic viscera.

When one observes that the compression of the cellular tissue is due to natural strain, it becomes obvious that with prolapsus uteri these areas have suffered greatest damage. Contained in this fascia are muscle fibers of a particularly elastic nature which aid the pelvic organs to return to normal position after physiologic displacement; consequently, those in whom such elasticity does not exist, or in whom the musculature has atrophied, are particularly disposed to prolapsus uteri.

In the erect posture, the direction of the rectal canal is downward and forward while that of the anal canal is at right angles. The angulation thus formed (the ampulla) is congenitally more marked in some individuals than in others. The exact rôle of Dénonvillier's fascia in the formation of the ampulla is not entirely clear, but it is felt that the relative infrequency with which these fibers can be demonstrated in procidentia is of significance.

With a patient in the recumbent position, the direction of the vaginal canal is downward and backward, or at an angle of approximately 90 degrees with the plane of the urogenital diaphragm. Throughout its greater length this potential canal is firmly encased in pelvic fascia which is, in turn, attached to the pelvic walls. The lateral and upper portion of this visceral support (the broad ligaments) is more cellular and broadly speaking may be considered the pelvic counterpart of the intestinal mesentery and, therefore, of relatively little value as a supporting structure. On the other hand, the base of the broad ligament, or that portion which partially retains the topography of the lateral fornices, commonly termed Mackenrodt's ligament, is not an independent structure but is an ill-defined portion of the endopelvic fascia.

One concludes from the foregoing that the pelvic organs are supported from below and not suspended from above, and, further, that the uterus, while never in a constant position, is maintained in one of relative anteversion by intraabdominal pressure on its posterior aspect, so directed by the development of the lumbosacral curve.

When lacerations occur in both sulci, or when an extensive paramedial episiotomy is performed, the fibers of the Luschka are divided, virtually enucleating the rectum from its attachment to the levator ani. The ampulla is thus left with but a poor support, yielding readily to the pressure of a loaded bowel. It becomes apparent that with a constantly overloaded rectum, the ampulla, improperly supported, becomes enlarged, bulging into the vagina until, eventually, it appears at the vaginal orifices as a rectocele. The process becomes a vicious one. From lack of normal support, the anorectal angle becomes distended into a culdesac because of such mechanical obstruction. Straining at stool in order to empty the lower bowel of its diverted contents causes greater distortion of the rectal ampulla until, eventually, the posterior vaginal canal is drawn down; the uterosacral ligaments and mesosigmoid supporting the vagina and rectum, in particular, are elongated.

With a prolonged second stage of labor, the uterosacral ligaments, as well as the pubocervical and other ligamentous supports of the uterus, become elongated, permitting subsequent retroversion, predisposing thus to descent. In instances where the uterosacral ligaments have not elongated from a prolonged or delayed second stage of labor, but where the ampulla is left unsupported, the gradual descent of the rectum not only reduces the length of the rectovaginal septum but separates the two canals, until ultimately the culdesac with its contents as an enterocele replaces the rectovaginal septum. The strain of such herniation is borne to a great extent by the uterosacral ligaments, which ultimately become incapable of retaining the uterus in its normal position.

SYMPTOMS OF PROLAPSE

While an appreciable descent of the pelvic viscera may have existed for some considerable time, it is only when the cervix protrudes from the vaginal canal that the patient urgently seeks relief. At the outset, one must differentiate the elongated hypertrophied cervix from true prolapsus uteri; in the latter, the length of the vaginal canal, with the patient in the upright posture, is reduced, while in the former such change is not observed.

Pain in the back is common to many conditions, and one should eliminate other possible causes of sacral or parasacral pain. In this, one is likely to correlate the symptoms with the pelvic findings. Exhaustive examination not infrequently reveals that the actual cause of the symptoms is one of deficient pedal arch support or mild sacroiliac strain. If no relief is obtained from a diagnostic pessary, symptoms may then be regarded as arising from some cause other than within the pelvis. In an effort on the part of the patient to divert

favors further descent. In the process of healing, following parametrial infection, smooth muscle is largely replaced by scar tissue, which, if supporting a heavy subinvolted uterus, may ultimately yield to the constant strain to which it is subjected. Only in rare instances is there a suggestion that parametrial infection per se contributes to procidentia. On the contrary, it is more likely that the management of labor, or the conduct of such delivery made more complicated by infection, is primarily at fault.

In over 80 per cent of the cases of prolapsus uteri active menstrual life has ceased. Just as some individuals at the menopause undergo more extensive changes of a general biologic nature than others, so, too, regressional changes in the pelvic supporting structures are subject to individual variations.

Loss of muscular tone as a result of defective carbohydrate metabolism is well known. In an apparently high percentage of patients admitted to the Gynaecological Service of The Montreal General Hospital for birth trauma, the fasting blood sugar value exceeded 0.120. The late H. M. Little observed that the frequency with which such a finding occurred seemed to be more than a mere accident. This observation will be commented upon, later.

With the menopause marked changes take place in all the pelvic structures; this is particularly noticeable in the reduction of the size of the uterus.⁵ In addition, there is usually considerable resorption of the supporting fat; more important, however, are the atrophic changes in the smooth as well as the striped supporting musculature.

In old age, there is a reduction in the lumbosacral curve. The intraabdominal weight in such cases is directed upon the pelvic floor. It is difficult to determine the importance of this factor in the production of prolapsus uteri, but the association with a reduced lumbosacral curve has been observed in such conditions.

Pariety seems to be of but little etiologic significance. Recently, a patient, aged forty-four, giving a history of having had 21 living children and 3 miscarriages, consulted me for metrorrhagia. On examination, a moderate rectocele and cystocele were found, with no evidence of either enterocele or prolapse. A vaginal hysterectomy for adenomyosis afforded an opportunity for further examination; the culdesac was found to be high, and the uterosacral ligaments were extremely well developed. On the other hand, Palmer Findley⁴ and others observed and reported complete prolapse in preadolescence, while prolapsus uteri, associated with congenital anatomical defects, is not uncommon.

Injury of a permanent nature to the rectal support during childbirth is often more real than apparent, as much irreparable submucosal damage to the perineal body results even from the so-called "ironing out" maneuver.

COMPLICATIONS AND SEQUELAE

With prolapsus uteri, mechanical obstruction of the urethra from strangulation results not only in an increase in residual urine but in "obstructive uropathy."²⁶ Mechanical distortion, while apparently limited to bladder and urethra, actually involves the entire urinary tract. As a result of prolonged partial or intermittent urinary obstruction consequent upon disturbance of the topography of the organs concerned, dilatation with subsequent infection of the upper tract of varying degrees occurs so that the depreciated renal function thus caused frequently becomes a more urgent problem than the existing prolapse. The corollary to such an observation is that in disturbed renal function in the female a thorough pelvic examination should be made to determine possible ureteral compression resulting from descent of the pelvic organs. The involvement of the ureter, with subsequent damage, is not a recent observation; Virchow, in 1846, stressed the possibility of hydroureter and hydronephrosis in prolapsus uteri, while Halban and Tandler⁹ maintain that some degree of dilatation of the ureters is almost a constant finding in genital prolapse. At autopsy, the condition was found by them in fifteen out of twenty-three instances. Brettauer and Rubin² found similar lesions in 80 per cent of their cases. The mechanics of such obstruction are not identical in all cases.¹⁰ With the altered relation of the pelvic viscera, the uterine arteries, being drawn down with the uterus, may possibly cause a sharp kinking of the ureters. But, as the bladder accompanies the uterus in its descent, it is improbable that ureteral obstruction is often thus caused, though Frank⁷ reported one instance of fatal uremia from pyonephrosis which he ascribed to this form of mechanical obstruction.

As the pelvic organs descend, there is considerable pressure on the ureters as they are stretched across the pelvic inlet, but the greatest compression takes place when the ureters are drawn with the hernia through the pelvic outlet; here the compression takes place between the medial borders of the levator ani. In any case, it is fortunate for the individual that such compression is rarely neither constant nor complete. When the bladder passes completely through the hernial ring, the obstruction to the ureters appears to be less as, in such cases, the ureters alone occupy the neck of the sac. The exact site of compression, while of academic interest, is of less importance than the fact that hydroureter and hydronephrosis are a common sequel to prolapsus uteri. Though pathologic dilatation of the ureters as evaluated by visualization is relative, we agree with Young²⁷ that the condition should be suspected in all cases of prolapsus uteri. The degree of permanent damage to the ureters and kidneys is in direct ratio to the duration of the vaginal hernia.

the intraabdominal weight so as to be borne by the pubis instead of by the poorly supported pelvic basin, the necessary postural hypercorrection eventually causes pain as a result of the constant strain upon the erector muscles. Though similar in nature, the symptoms in such a case are not actually from displacement of the pelvic viscera.

The degree of pain is variable, depending on the underlying cause of the sacropubic hernia. If of a congenital nature as observed in the nullipara, the pain in the back is at a higher level, for in such cases there is no traction on the so-called rectosacral ligament but rather on the mesentery of the small bowel. On the other hand, if the prolapse be traumatic in origin, the pain thus caused from traction on the rectum, which in turn is attached to the sacrum through the medium of the mesosigmoid, may be and often is intense. The relative absence of pain in the sacral region should lead one to suspect an existing congenital enterocele, even in the presence of an obviously badly damaged birth canal.

With advancing years, owing to the sedentary life, and also to the partial disability resulting from a poorly supported pelvic floor, constipation becomes distressing, virtually reaching the point of rectal obstruction. The process becomes a vicious one; with forcing and straining the ampulla becomes larger until, at last, evacuation is possible only if the rectum be digitally supported.

Hypertrophy and elongation of the cervix are present in the vast majority of instances of prolapse. Possibly the cervical enlargement contributes primarily to the descensus but, more probably, it develops as a result of prolonged congestion and irritation. Strangulation of the hernia occasionally occurs to such a degree that reduction becomes difficult, even with the patient in the knee-chest position or the exaggerated Trendelenburg position.

In the absence of pathologic findings in the urine, urinary frequency, due to extravescical mechanical pressure, may be associated with various degrees of birth trauma. Such irritation to the trigone is often caused by a rectocele, yet one should bear in mind that urinary symptoms of this character more frequently accompany an enterocele.

Prolapse may exist without any apparent damage of the urethral support and, in such cases, incontinence is not necessarily present. On the other hand, according to a urologic colleague,¹⁷ if there is a sagging or pouching of the bladder floor the condition is not unlike the "bas fond" which is often found associated with prostatic enlargement. When relaxation involves the urethral support, distressing incontinence may follow. In the event that urethral and vesical support are both defective, it is difficult to explain the absence of urinary frequency or residual urine in a goodly percentage of cases with complete prolapse.

The possibility of carcinoma¹⁴ developing on the everted pelvic viscera should be borne in mind; while only one such case was observed and reported from Johns Hopkins Hospital, it is worthy of note that, within the past ten years, two patients with carcinoma of the hernia were admitted to our service.

TREATMENT

In a recent communication before this Society,³ certain prophylactic measures were outlined which, when adopted, are valuable in minimizing the permanent damage of the birth canal incident to parturition.

When prolapsus uteri becomes apparent, supporting mechanical devices are, as a rule, employed only as a temporary measure while awaiting preparation of the patient, or in those patients who are unsuitable for surgical treatment. As with other hernias, a permanent cure occasionally follows continued support of a sacropubic hernia.¹⁶

It is of historical interest to note that vaginal plastic procedures owe their birth to Marshall Hall¹⁵ who, in 1831, observed permanent cures following prolonged use of pessaries.

A definite principle¹ should underlie all operative procedures, yet each case should be considered individually as no one method is a panacea.

Any operation which essentially consists of suspending the uterus without properly reconstructing the vagina is anatomically unsound. Such procedures give the bladder a hammock-like support which results in an actual increase in residual urine, with its usual sequelae.

Interposition operations have been employed by us for years but the procedure has been reserved, mainly, for cases of true cystocele, and not for those with marked relaxation or elongation of the ligamentous supports of the uterus responsible for permitting prolapsus uteri. Interposition operations may temporarily relieve the symptoms but such a procedure is rarely successful in curing sacropubic hernia.

Vaginal hysterectomy not only removes the uterus, which not infrequently is the site of some subsequent pathologic lesion, but, at the same time, the essential supporting structures are rendered more accessible for the purpose of reconstruction.

In order to maintain the normal direction of the vagina so that the bladder may be supported in its proper position, continuity of a relatively taut fascial plane, extending from the posterior aspect of the pubis in front of the pelvic wall posteriorly, is of vital importance. By removing the uterus, the pouch of Douglas, which is frequently unusually deep, may be shortened, while the arch formed by the junction of the two uterosacral ligaments, anteriorly, and the rectum, posteriorly, is easily reduced in size, as it is at this site that recurrent

Normally the opening of the ureter into the bladder is through a zigzag course but, when the ureter is unduly stretched and the bladder wall thinned out, the normal valvelike effect from the peculiar course of the ureter through the bladder wall is lost, permitting the infection in the bladder (the natural sequela of residual urine) to ascend. Subsequent kidney damage of a greater or less degree almost invariably follows.

As stated previously, the complications and sequelae of prolapsus uteri may be many, leading in certain instances to serious disturbances in metabolism. Whether these disturbances always result from the prolapse or, on the other hand, are accidental findings, such biologic changes are, nevertheless, important. Often an alternative type of repair must be chosen, or the technic modified to suit the case, as such conditions materially retard postoperative progress.

Though previous reference has been made to disturbances in metabolism encountered in prolapsus uteri, I especially wish to refer to that of carbohydrate metabolism. It is particularly worthy of note that, while in only 28 instances out of 378 admissions for birth trauma was there any evidence of glycosuria, fasting blood sugar estimation revealed some interesting data. In 378 patients admitted for some degree of damage to the birth canal, the fasting blood sugar averaged 0.128. One hundred fifty-six patients, or 40 per cent of them, had blood sugar values over 0.120 on admission. Of those with elevated readings 78 per cent showed definitely disturbed carbohydrate metabolism. There were 12.9 per cent of all patients admitted for birth trauma who had fasting blood sugar values exceeding 0.150, a definite indication of pathologic carbohydrate metabolism.

Further significance can be placed on these observations when the postoperative results are analyzed. In 1926, I. M. Rabinowitch¹⁹ stressed the importance of blood sugar determinations in surgical conditions generally. In a recent survey in the Gynaecological Service of The Montreal General Hospital, C. V. Ward²⁴ showed that the incidence of primary union in diabetic patients following vaginal repair was over 93 per cent, identical with that of nondiabetics, when pre- and postoperative treatment included appropriate diet, with or without insulin, as found necessary by the Department of Metabolism. Equally good results follow intraabdominal procedures when similar precautionary measures are observed.

Ulceration of a refractory nature is common, and seriously delays operative repair of any sort. Severe hemorrhage from ulceration is not uncommon, and is extremely difficult to control; recently a diabetic patient was admitted to our ward in whom a rapidly developing ulcer bled so profusely that her family physician was able to arrest the hemorrhage only by applying a tourniquet about the base of the hernia; on examination, it was found that the ulcer was carcinomatous.

All patients undergo a preoperative interval of observation, usually extending over a period of from three to five days. If a marked hydro-nephrosis or bilateral pyelitis is detected, prolonged bed rest in the dorsal position with forced fluid is insisted upon, augmented, in certain instances, by bladder lavage or continuous bladder irrigation. If the infection is refractory and pus cells of more than 25 to the H.P.F. persist, the operation is then temporarily postponed.

In most cases, decubitus ulcers, when present, subside with daily hot sitz baths to the hernia, followed by drying of the part. The prolapse is replaced after each bath, and an acriflavine emulsion tampon is reinserted. Daily douches of lactic acid (drams 1 to 1 pint) are



Fig. 2.

prescribed for all patients of this group. This procedure does much to reduce the incidence of postoperative vaginal infection, as well as to hasten healing of decubitus ulcers.

Hormone therapy in the form of estrin, when administered for one week prior to operation, reduces the possibility of infection which is likely to follow any surgical procedure in the presence of a senile vaginitis.

TECHNIC OF VAGINAL HYSTERECTOMY

The immediate preoperative medication consists of Nembutal gr. iii, administered orally forty minutes before leaving the ward. Spinal anesthesia with novocaine crystals has proved particularly satisfactory. The cases with high blood pressure tolerate this type of anesthesia particularly well as do those with

herniation occurs. As part of the surgical procedure both the anterior and posterior walls of the vagina are repaired, after the manner herein described.

PREOPERATIVE INVESTIGATION

On admission to the hospital, an exhaustive history is taken and a general physical examination of the patient is made, in order to elicit the existence of any pathologic process other than that of prolapse.

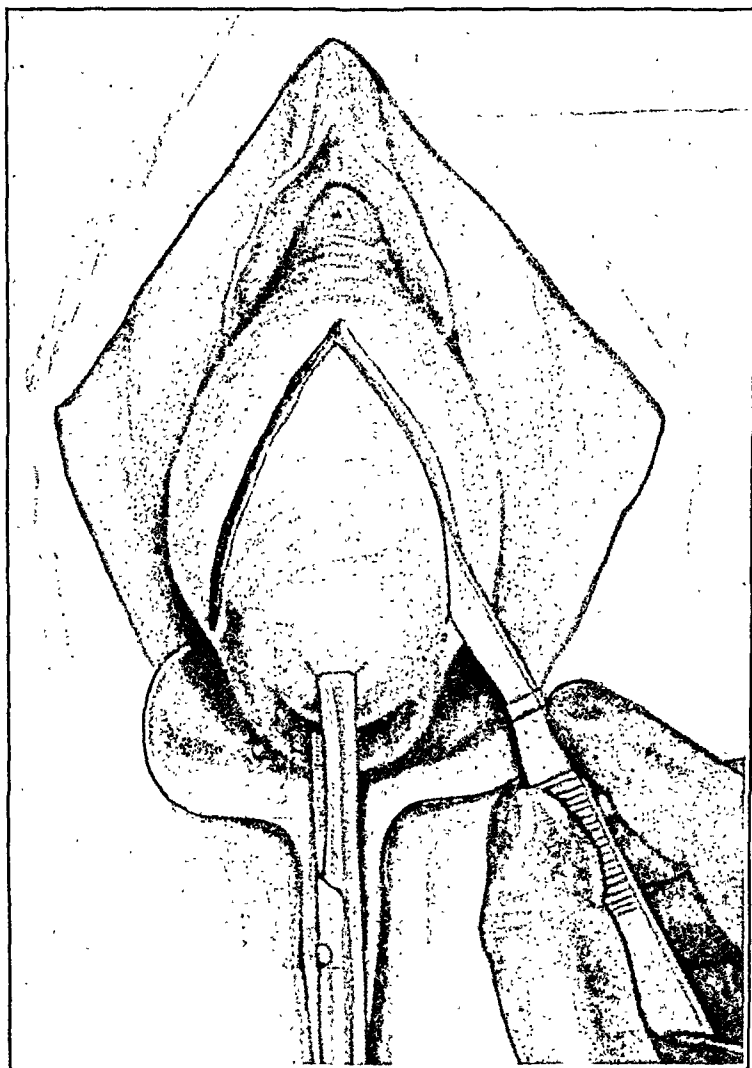


Fig. 1.

If a coexisting lesion is suspected, the respective departments are requisitioned for investigation of the part in question. In addition, routine blood Wassermann, urinalysis, complete blood count, and sedimentation rates are obtained, while fasting blood sugar, urea, creatinine, and urea clearance and concentration factors are determined. We have been uniquely fortunate at The Montreal General Hospital in having the close cooperation of the Urological Service, where cystoscopic examination of the patient, as well as visualization of the entire urinary tract, either by retrograde or direct means, is carried out.

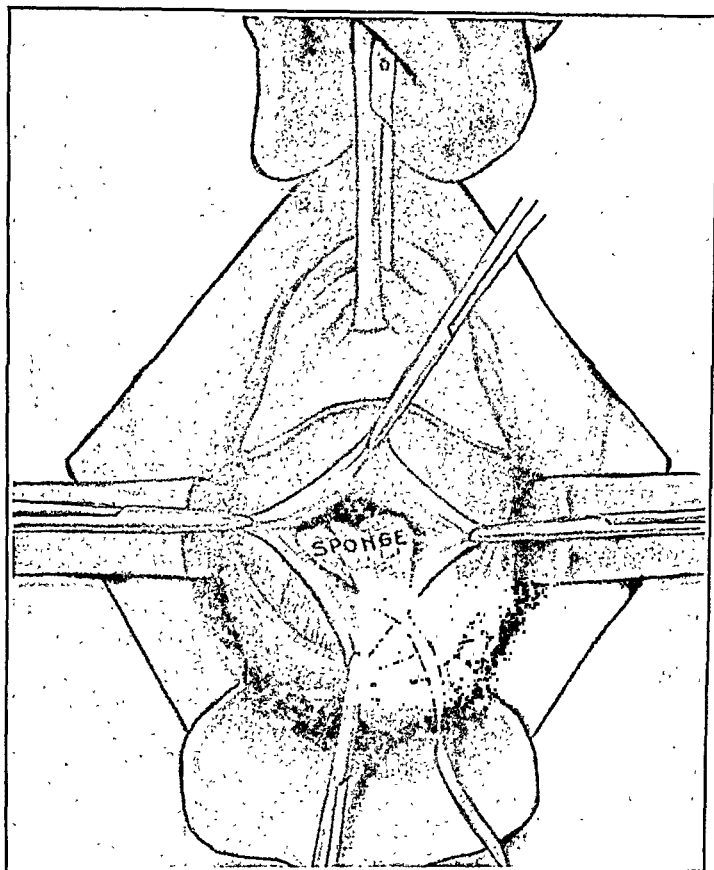


Fig. 4.

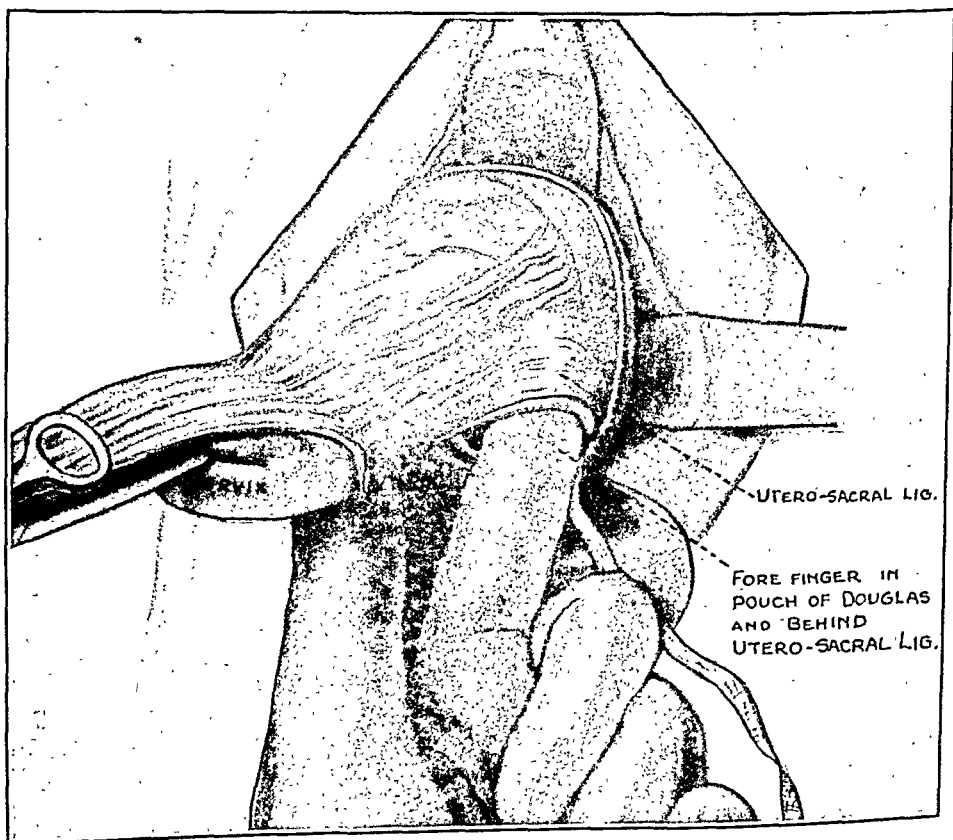


Fig. 5

various forms of debilitating conditions, as evidenced by the absence of post-pulmonary and other complications, and seem to justify this form of anesthesia. In addition there is infinitely less "oozing" of blood in the field of operation with this form of anesthesia.

In the lithotomy position, the entire area is thoroughly sterilized with iodine 2 per cent, and after catheterization, the patient is draped in the usual manner. With a tenaculum the cervix is drawn down, while with an Allis forceps grasping the mucosa immediately posterior to the urethra, the anterior vaginal wall is put on a stretch. A racquet-shaped incision through the mucosa is made, extending from the urethra and surrounding the cervix (Fig. 1). The mucous membrane is then pushed upward, the base of the bladder being partially exposed is elevated

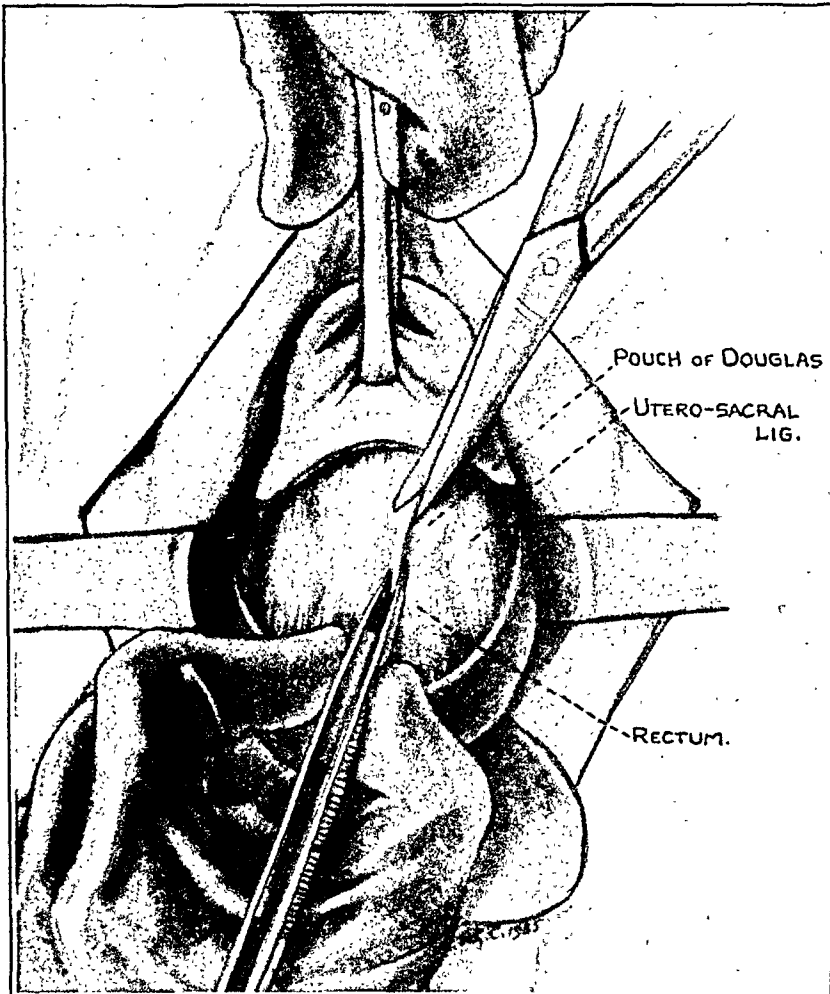


Fig. 3.

from the anterior aspect of the uterus but, to minimize bleeding, is not separated from the mucosa of the anterior vaginal wall (Fig. 2). On exposure of the peritoneum of the culdesac, an incision is made in the peritoneum (Fig. 3), and a small abdominal towel saturated with 5 per cent aqueous acriflavine is inserted into the pouch of Douglas (Fig. 4); this insures the walling off of the contents of the pelvis and, at the same time, absorbs any soiling which may enter through the incision. With the index finger of the left hand inserted through the incision (Fig. 5), the uterosacral ligament, on the left side, is clamped and, as the fundus is approached, the finger is swept around behind the fundus of the uterus so as to push it forward (Fig. 6). When the uterovesical fold of peritoneum is put on the stretch it is incised, and the fundus of the uterus is then delivered. The remain-

ing portion of the broad ligament, including the uteroovarian ligament and the fallopian tube, is then clamped. The uterus is turned laterally to the right in a battledore fashion, and the right broad ligament clamped in a manner similar to that of the left (Fig. 7). All bleeding points are then ligated. The peritoneum is now grasped with Allis forceps. The culdesac is next examined and, if the pouch of Douglas extends far down toward the perineal body, a purse-string of No. 2 chromic catgut is inserted particularly high (Fig. 8), after the manner of Phaneuf.¹⁸ The redundant peritoneal tissue is then removed. The free ends of the purse-string are tightened and tied, while the acriflavine tampon is withdrawn. The ends of the purse-string are not cut but are left long and held for subsequent use.

It will be noted that thus far in this procedure the bladder has not been separated from the mucosa of the anterior vaginal wall in order that the operative

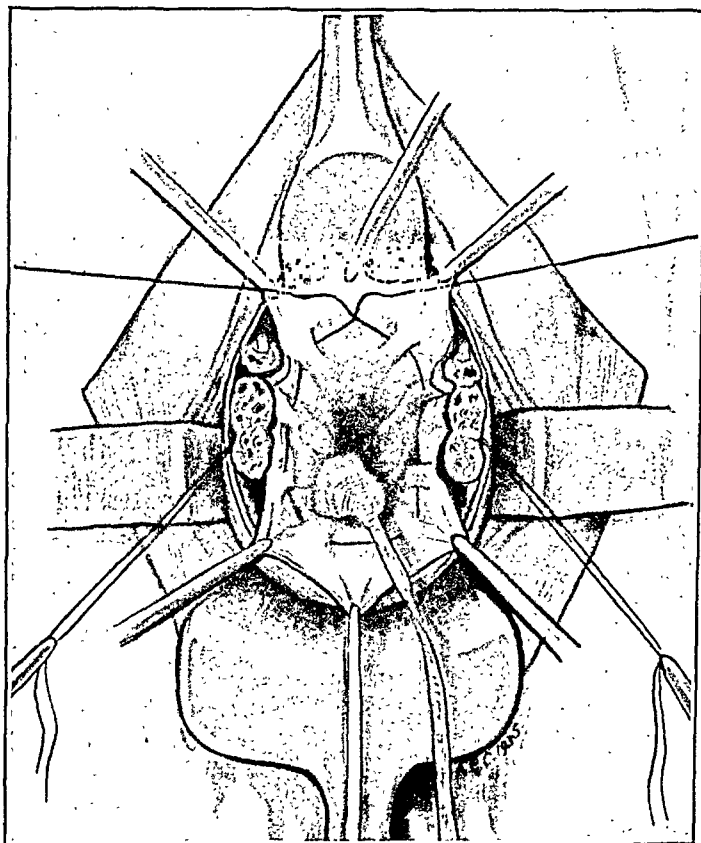


Fig. 8.

field may be kept as dry as possible. The peritoneal cavity having been occluded, the mucous membrane of the anterior vaginal wall is grasped with a series of clamps and with a sponge is gently separated from the bladder (Fig. 9). The uterosacral ligaments are then sutured into the pubocervical fascia (Fig. 10), while the free ends of the uncut purse-string suture of the peritoneum are brought around the uterosacral ligaments and tied on the inferior surface. This is done so as to occlude any possible "dead space," and to retain the normal relationship of the lower end of the culdesac to its supporting structure. The uterosacral ligaments are sutured to each other so as to reduce the size of the arch formed by their approximation; subsequent herniation is thus prevented (Fig. 11). The redundant mucosa of the anterior vaginal wall is then resected (Fig. 12), and closure is made with nine interrupted No. 1 catgut sutures. An alcohol tape, one and one-half feet long, is then inserted into the vaginal vault to insure drainage (Fig. 13).

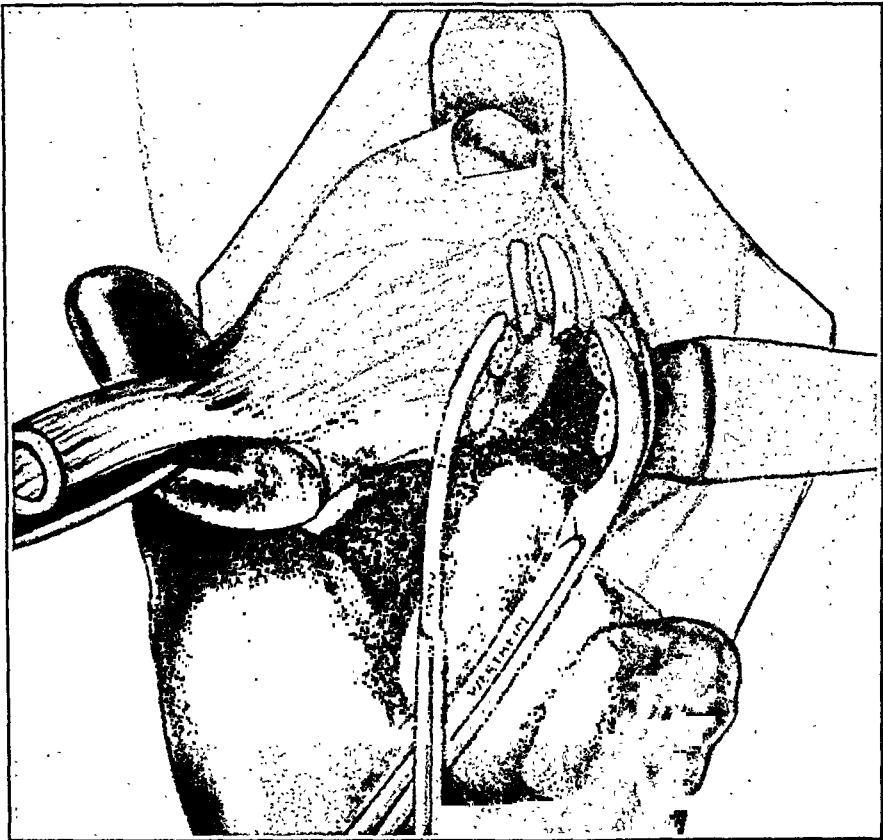


Fig. 6.

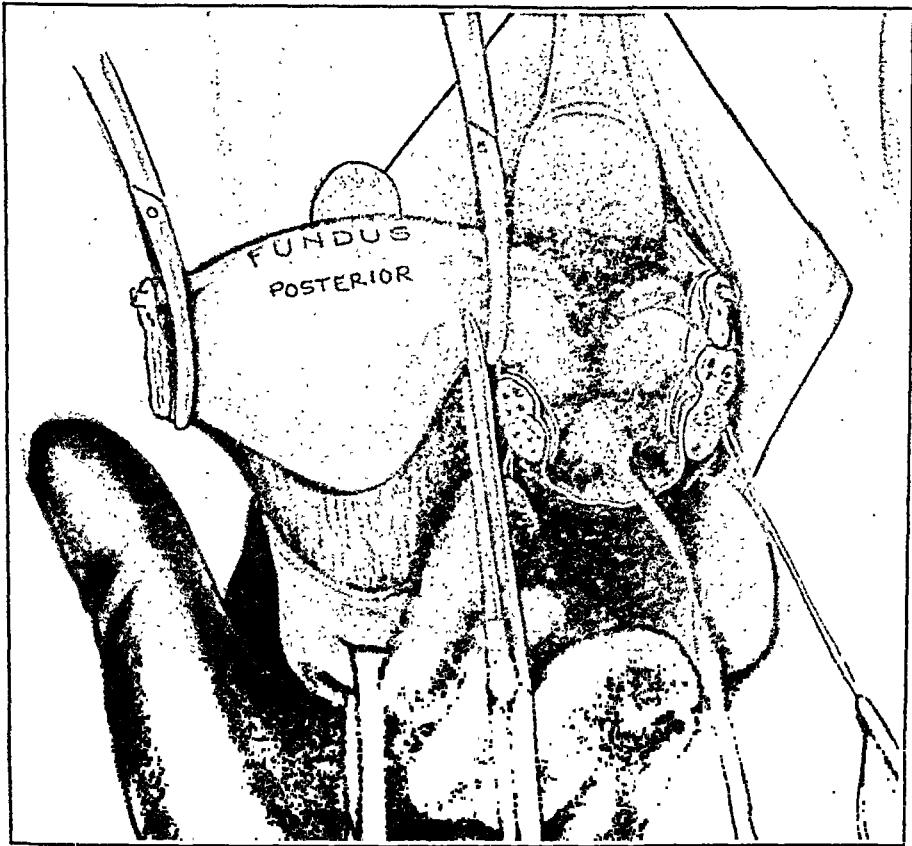


Fig. 7.

The posterior vaginal wall is then repaired. After having made a transverse incision at the mucocutaneous junction, the mucous membrane is elevated (Fig. 14) and, with two clamps,³ a V-shaped portion of mucous membrane of the vagina is outlined and removed.¹⁵ The perirectal cellular tissue is then approximated with interrupted catgut sutures. After approximation of the levator ani muscles, the urogenital diaphragm is then reconstructed. Closure is made in the vaginal floor by double continuous No. 1 catgut sutures.

At this juncture, the cut or damaged ends of the sphincter vaginae are drawn backward, and attached to the sphincter ani externus. Such reconstruction of the perineal body prevents the subsequent perineal scar which inevitably follows the perineotomy being drawn forward by the action of the sphincter vaginae and, also,

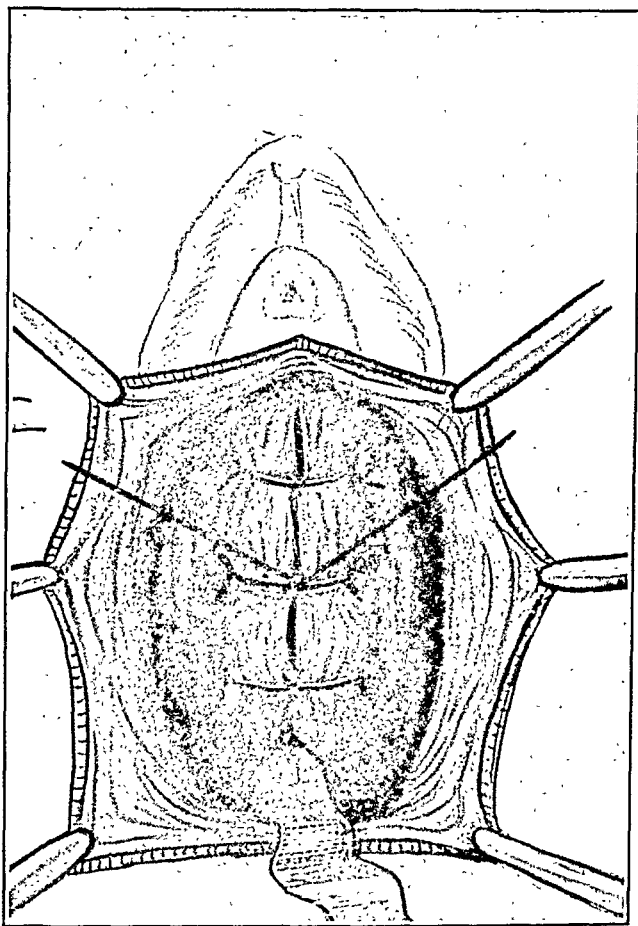


Fig. 11.

obviates the distressing condition of the so-called "sacral anus." The anal canal when held well forward obviously reduces the anorectal angle, an essential detail to insure success of any form of perineal reconstruction. The superficial structures of the perineum are finally brought together with a subcutaneous No. 1 catgut suture; an indwelling catheter is then inserted.

POSTOPERATIVE CARE

As part of the technic of spinal anesthesia, the patient is kept in the dorsal decubitus position for twenty-four hours, which position, fortunately, is the one of choice to insure good kidney drainage. During this time sedatives are freely administered as required. Vaginal packing inserted at the time of operation is removed by the end of forty-eight hours.

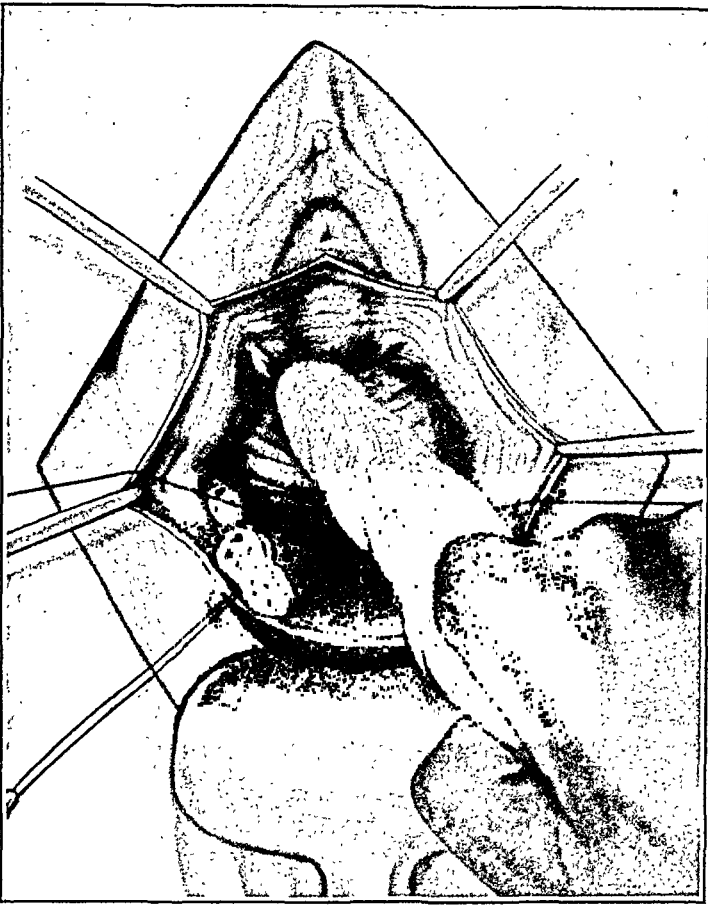


Fig. 9.

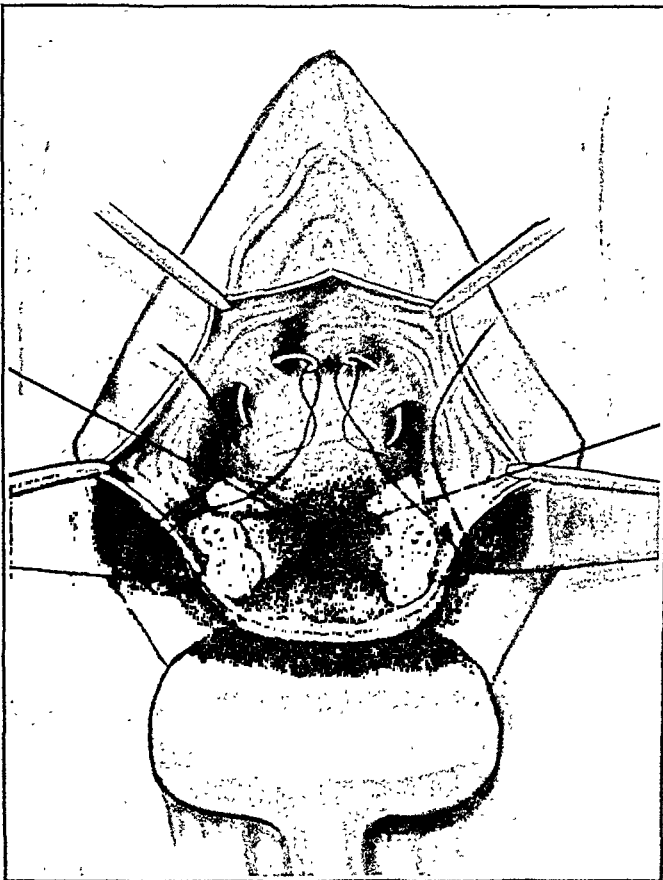


Fig. 10.

Vaginal hysterectomy is not a new procedure;^{11, 13} according to the late George Gellhorn,⁸ Robert Battey of Rome, Georgia, in 1876, was the first to approach the pelvic organs through the vaginal canal. This type of operation has of late become increasingly popular, but, although a satisfactory surgical measure in the treatment of prolapsus uteri, like all other operations it has its limitations.

Often patients with procidentia have symptoms suggestive of an intraabdominal pathologic lesion. In such cases, because of the limited

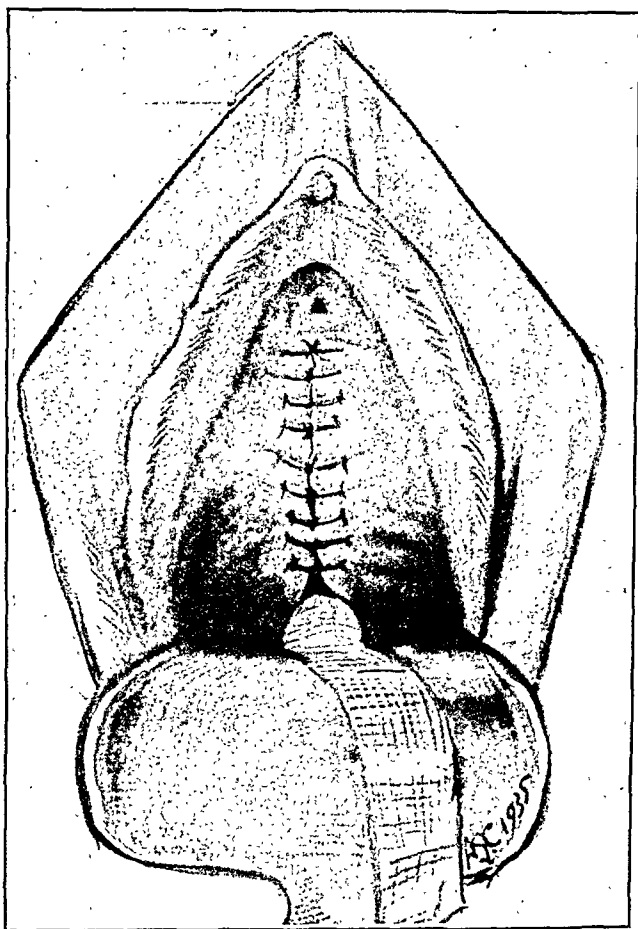


Fig. 13.

field exposed through the vaginal route, it is considered wiser to perform a laparotomy, either at the same time the birth canal is repaired or at a subsequent date, rather than attempt too broad a dissection from below.

In the procedure herein described, I have endeavored to stress the importance of a knowledge of anatomy of the pelvic structures. I should like to make it clear that, while it is impossible to dissect and identify the various portions of the fibromuscular fascia, certain areas are subjected invariably to greater strain, and in one's reconstruction these so-called cardinal ligaments must be so arranged as to give adequate support to the abdominal structures dependent upon the pelvic basin for support.

The indwelling catheter prevents undue strain on the suture lines from over-distention of the bladder. It is not disturbed for the first four days, thus obviating repeated catheterizations, which would otherwise be probably imperative during the period in which glucose saline is freely administered, intravenously. Daily vesical irrigations with sterile boracic solutions are carried out, while after each irrigation 5 c.c. of a 20 per cent solution of argyrol are instilled into the bladder. When the catheter is finally removed (on the fourth day), the patient is catheterized every eight hours if necessary. Following voiding, the patient is catheterized and, if on two successive occasions the residual urine does not exceed 30 c.c., this procedure is discontinued.

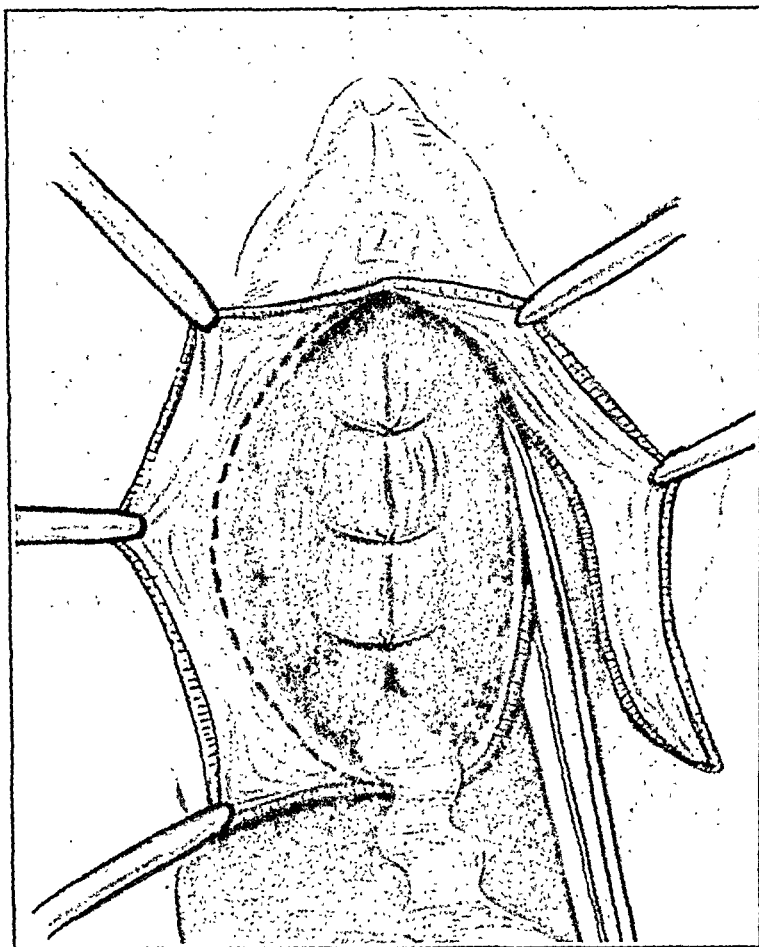


Fig. 12.

When the patient can tolerate a mixture of milk of magnesia and liquid paraffin, she is given one ounce of each twice daily, in order to encourage early spontaneous bowel evacuations. On the third morning (postoperatively), a soapsuds enema is administered.

Daily douches of lactic acid (drams 1 to the pint) are given, after the removal of the packing. Patients are permitted out of bed by the thirteenth day, and discharged some three or four days later.

Experience has shown us that a fasting blood sugar above 0.120 is inimical to healing of perineal wounds, hence all patients with a blood sugar value between 0.120 and 0.130 are routinely given five units of insulin, three times daily. Those whose carbohydrate value exceeds this are referred to the Department of Metabolism which places the patient on the strictest regime: doses of insulin varying as indicated by fasting blood sugar reading.

Abscess in the vaginal canal necessitating drainage occurred in three of the earlier cases, probably owing to the faulty occlusion of potential "dead spaces." The presence of glycosuria in two of these cases no doubt contributed to the infection. The only death resulted from peritonitis in a patient with a virulent form of streptococcal pyometria and senile vaginitis. We feel that had we employed estrin therapy, preoperatively, in this case such a result would have been averted.

A late postoperative complication was the recurrence of an enterocele²⁵ in two cases, which demonstrated to us the absolute necessity of reducing the size of the rectal cleft in the endopelvic fascia.

The above complications occurred in the earlier cases, which impressed upon us the importance of certain features in the technic and conduct of this type of case which I have endeavored to stress.

COMMENT

Prolapsus uteri results from either congenital defects in the structures supporting the uterus or from damage to these tissues incidental to childbirth, or both.

A thorough understanding of normal pelvic anatomy is essential in order to comprehend changes that occur in the topography of the pelvic contents incident to the defects in the supporting structures which permit procidentia.

Since sacculation of the bladder, hydroureter, or hydronephrosis resulting from procidentia is accompanied by infection of the entire urinary tract, complete blood chemistry should be obtained. Similarly visualization (either direct or retrograde) of the urinary tract is essential.

Vaginal hysterectomy with repair of the birth canal is a satisfactory surgical measure, the essential features of the technic employed being spinal anesthesia, a relatively bloodless field, protection of the peritoneal cavity, reduction in size of the pouch of Douglas, occlusion of all "dead spaces" and reconstruction of the pelvic cellular tissue. The importance of the uterosacral ligament is particularly emphasized.

Vaginal hysterectomy is not recommended for prolapsus uteri when there are abdominal symptoms, or where any palpable abdominal or pelvic lesion is detected, or where so-called senile vaginitis exists.

From the fact that in prolapsus uteri the extent of the damage to the pelvic or other organs is not identical in any two cases, the term "percentage cures" is obviously fallacious. Unfortunately, there is no "yardstick" by which one can measure the actual damage from the anatomical derangement present in sacropubic hernia. While the support to the pelvic structures may be satisfactorily reconstructed, from an anatomical standpoint there is no proof that the organs involved will return to their original physiologic state. We therefore must appraise our results largely on the permanency of our reconstruction but, more particularly, on the subsequent well-being of the patient. In the study of prolapsus uteri, more than in any other gynecologic condition, one is forced to realize the interdependence of the various branches of

RESULTS .

During the past two and one-half years vaginal hysterectomy was performed in 70 cases, 66 of which were for birth trauma, with an average age of 53.1 years, the youngest being thirty while the oldest was seventy-two. The average parity was

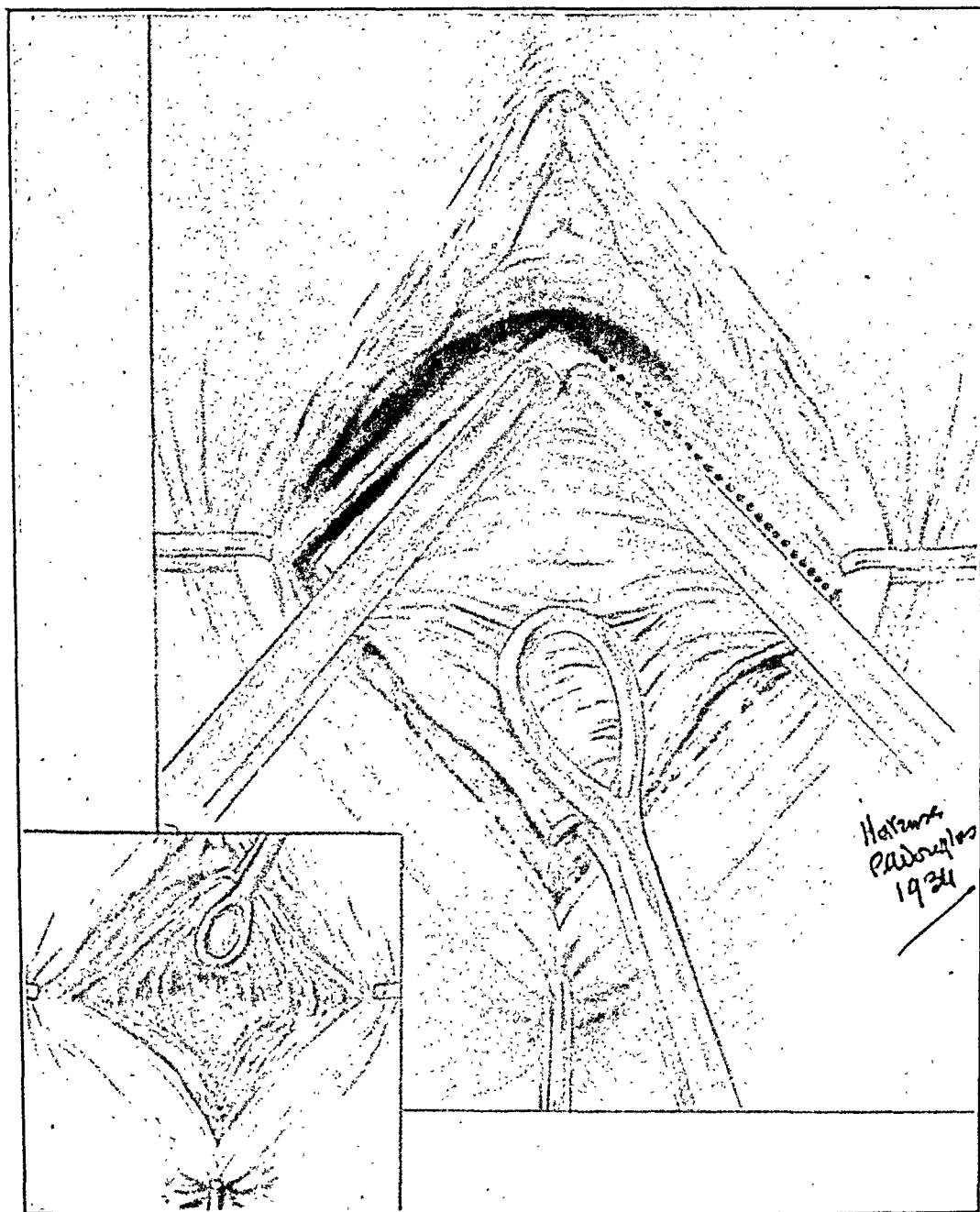


Fig. 14.

Fig. 15.

4.7, including one patient who was a para xxiv, and three nulliparas, all averaging a hospitalization of eighteen days.

Postoperative complications, in the form of varying degrees of urinary tract infection, were present in 36 per cent of cases. A great number of these cases had a pre-operative pyuria; the operation probably merely caused an acute exacerbation of a temporarily quiescent infection.

of the anterior vaginal wall is excised, closure being performed by silkworm-gut sutures. Absorbable or buried sutures must not be used on account of infection incident to the slough from the clamp method of removing the uterus. A marked rectocele can best be taken care of a little later, after retraction of the vaginal walls has taken place from the hysterectomy. This repair of the rectocele is performed before the patient leaves the hospital.

DR. W. SCHILLER, VIENNA, AUSTRIA.—With the changes caused by chemical irritation, such as the urine flowing over the surface of the uterus; by mechanical irritation resulting from friction between the exposed uterus and the thighs; by thermic irritation from exposure to variations in the temperature of the air, it would be expected that carcinoma would develop more easily and frequently in procidentia and prolapse than in the normally placed uterus. I have examined the specimens from a large number of cases of prolapse of the uterus and also of carcinoma of the cervix and among those cases I found altogether only seven cases of prolapse associated with carcinoma of the cervix. Five of these cases have been published by Hoegler and since then I have discovered two more cases. This leads to the conclusion that in prolapse the incidence of carcinoma is much lower than in uteri normally situated.

The few instances of carcinoma occurring in prolapse deserve explanation. The change observed in the epithelium in prolapse is a keratosis which is the physiologic reaction that serves to protect the organ against the external insults resulting from its position. We know that the parts of the skin that physiologically have the highest grade of keratinization, as the palm and sole, have a lower incidence of carcinoma than the parts of the skin that are less keratinized, for example, the face.

On the other hand, there are certain types of hyperkeratosis that have a tendency to change to carcinoma, as in chronic intoxication. It is a very interesting fact that many years ago the use of Fowler's solution was abused by its being given in high doses daily for many years. But such patients used to develop hyperkeratotic areas, especially on the forehead, and eventually the arm and those areas showed a marked tendency to change into carcinoma. This observation leads to the conclusion that we must distinguish between two types of hyperkeratosis as regards their tendency to develop carcinoma, the physiologic type being a reaction against the mechanical and drying-out influence; and toxic hyperkeratosis in consequence of chronic administration of arsenic. The first type means a certain protection against carcinogenesis.

After all we must admit that in cases of prolapse the probability of carcinoma is much lower than in normal women, for whereas in normal women the incidence of carcinoma of the cervix amounts to 3 per cent, the incidence of carcinoma in women with a prolapse amounts to only 0.5 per cent, according to my statistics. This is not opposed to the proposal to treat patients with procidentia by vaginal hysterectomy. We should never support this proposal, however, by stating that these patients have a higher incidence of carcinoma than do women with normally placed uteri.

DR. W. W. BABCOCK, PHILADELPHIA, PA.—While I have been very much interested in vaginal hysterectomy and have performed about 90 per cent of hysterectomies by this route, I have not felt that vaginal hysterectomy played a very important part in the treatment of procidentia. Indeed, it has been my impression that if the uterus is of a fair size it often is wise to do an interposition operation so as to raise the bladder and stabilize and fix the anterior vaginal wall.

At the same time, I think there is no question that one can perform a vaginal hysterectomy with an associated plastic operation with very excellent results in procidentia. A small senile uterus is of little or no value as an interposed organ, while its removal enables one to obtain support to the vagina from the broad and uterosacral ligaments. In every case it seems very important to secure a very high pelvic floor so that the resultant of forces that arise when the patient is standing will deflect the pressure forward upon the pubis. The weight is thus largely supported by the bone rather than by the soft parts.

medical science. A fair understanding of these is necessary in order to obviate the manifold failures so frequently resulting from surgical treatment of this most distressing condition.

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1414 DRUMMOND STREET

DISCUSSION

DR. J. W. KENNEDY, PHILADELPHIA, PA.—In 1926 at our meeting in Chicago, when I discussed vaginal hysterectomy as the best treatment for uterine prolapse, I met with unyielding opposition. The opposing arguments were based upon the fact that the indwelling uterus could be used through some type of fixation operation, either for the purpose of elevating the bladder by attaching it to a higher point on the uterus or the organ might be used in executing the interposition operation.

Although there may appear to be a marked difference in Dr. Campbell's and my methods of treatment of prolapsus uteri, yet in the substantial principles involved, we are in accord. In each the surrounding uterine ligaments are dealt with so as to elevate the vaginal fornix and bladder to their normal positions. What Dr. Campbell accomplishes by suture or plication of ligaments, we execute by the clamp method, which permits the contraction and retraction of all uterine ligaments after the clamps have been removed. This allows the uterine ligaments to retract toward their bony attachments, thus pulling or elevating the vaginal fornix and accompanying bladder to their normal locations. The retraction of the ligaments, when the extremities are freed from the clamps, is, however, far greater than can be obtained by suturing their extremities together after vaginal hysterectomy. In marked prolapse of the uterus and bladder, those procedures, such as the interposition operation or elevating the bladder by stitching the same to a higher point on the uterus or broad ligaments, will fail in a large percentage of cases on account of the overstretched and elongated ligaments and will not give sufficient shortening to the sustaining structures with the indwelling uterus. The uterus is the keystone of the prolapsed and elongated arch (uterus and broad ligaments) and when it is removed by the clamp method, the arch is shortened, the keystone (uterine position) is filled in with fibrous tissue, all the uterine ligaments retract to their bony attachments, thus elevating the vaginal fornix and bladder to their normal positions.

In the complete procidentias, with bladder and vaginal wall prolapsed between the patient's thighs, after finishing the vaginal hysterectomy, we immediately perform an extensive cystocele operation. In this a large triangular area of the entire thickness

BILATERAL TRANSPLANTATION OF THE URETERS OF THE FEMALE

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TRANSPLANTATION of the ureters to the pelvic portion of the colon is now recognized as a standard surgical procedure for the treatment of exstrophy of the bladder. It is very successful and can be performed with a low mortality if there are no complicating conditions in the upper part of the urinary tract. The good results obtained in the treatment of this condition have been the stimulus for transplanting the ureters of women in the treatment of conditions in which the urinary bladder has been rendered useless by traumatism or by disease. Those conditions I wish to consider are huge vesicovaginal fistulas, chronic interstitial cystitis with secondary contraction of the bladder, and certain carcinomas of the bladder.

The technic employed for transplantation of the ureters at The Mayo Clinic is that of C. H. Mayo, which utilizes Coffey's principles of transplantation of the common bile duct. This necessitates the transplantation of one ureter at a time; the right ureter is transplanted first, and the left ureter is transplanted not earlier than two weeks after transplantation of the right ureter.

Briefly, the method consists of intraperitoneal isolation of the right ureter and its division as near the bladder as possible. The parietal peritoneum is closed by a running suture, but only loosely around the ureter. An incision about $1\frac{1}{2}$ inch (3.77 cm.) long is made in the longitudinal band of the rectosigmoid; this incision extends down to the mucosa but not through it. The submucosa is separated from the mucosa slightly on each side, and at the distal end a puncture is made through the mucosa; this puncture is just large enough to admit the ureter. The lower end of the ureter is partially split for a distance of about 0.6 cm. and a suture is tied to it. About 2 inches (5 cm.) of the short end of the tied suture is threaded into the ureter as a guide for the urine. The ureter is drawn through the opening in the bowel by this suture, the needle emerging through the bowel about 1.5 cm. beyond the lower end of the incision in the sigmoid. It is anchored to the peritoneal surface of the bowel. The cut edges of the muscular wall of the bowel are united over the ureter by as few interrupted sutures as possible. A continuous row of sutures next covers the entire incision and all previous sutures as additional protection.

I was interested in the author's method of completely closing the peritoneum in vaginal hysterectomy. I have had considerable trouble in perhaps 10 or 15 per cent of the cases in which the peritoneum and vagina were entirely closed. A secondary infection in the pelvis often develops about seven to ten days after the operation and this necessitates reopening. As a result, for years we have not closed the pelvic opening and have carried gauze drains into the pelvis in all cases. Possibly Dr. Campbell avoids the pelvic infection by bringing the pedicles outside the peritoneum and not closing the vaginal wall. I hope he explains this.

As to his 33 per cent pyurias, we have felt that infections of the bladder have been largely eliminated by keeping a retention catheter in for three or four days after all operations where the uterus is removed or when an operation for procidentia is done. In this way retention of urine is avoided. The bladder is irrigated daily and silver protein instilled when the catheter is finally withdrawn.

PROFESSOR MILES PHILLIPS, SHEFFIELD, ENGLAND.—I have been doing this operation since 1910 and have performed it more than 500 times. It is not done exclusively for procidentia, but combined with double colporrhaphy is employed for such indications as the smaller fibroids, senile pyometra, lacerated cervix, or badly infected cervix.

The operation is especially valuable in those cases where there is a congenitally deep pouch of Douglas. That is a very important factor in many cases, not only in the spinster but in other women who may have had only one or two children.

I do not excise the peritoneal sac now but purse-string it as high as possible, leaving the eventrated plaque of peritoneum to help fill the space between the upper vagina and rectum.

I always drain the potential space outside the peritoneal cavity. I used to do that with gauze or rubber, but do it now invariably, and I think most successfully, by leaving the catgut sutures which unite the uterosacral ligaments to the angles of the vaginal vault and to each other, with long projecting ends. I now have none of those small abscesses nor anything in the nature of a peritonitis. We use only plain catgut and the ligatures come away very easily.

In my last 150 private cases there was no mortality. Unfortunately, the next patient succumbed to an accident not directly connected with the operation, having developed a pulmonary abscess associated with the anesthetic. The mortality is therefore very low, and the painlessness of convalescence is very striking.

I used the clamp method occasionally in 1908, but I have not done so recently.

I think the retaining catheter is very useful, but a most valuable addition is sodium mandelate to prevent *Bacillus coli* infection. Its use was begun by Rosenheim of London and has met with great success. I anticipate an increasing use of vaginal hysterectomy in the treatment of prolapse.

DR. CAMPBELL (Closing).—In answering Dr. Babcock's remark, where birth trauma is limited to cystocele, the interposition operation is reserved. Suspension of the uterus does not cure genital prolapse. On the contrary, such a procedure converts the anterior vaginal wall into a hammock, thereby increasing the residual urine and further damaging the kidney. The pelvic organs are supported from below and not suspended from above.

We have not had an infection in the culdesac except in one case and that was where I did not close the culdesac. I feel that infection depends in a large measure upon the way we treat our patients preoperatively. As I said before, if we use estrin, especially if senile vaginitis is present, we will increase the circulation in the vaginal mucosa and thereby reduce the morbidity.

The abscess formation in the vaginal vault, as a rule, results from dead space. If there is much dead space left between the peritoneum and the reconstructed pelvic floor, there will always be an abscess. I hope at some later time to offer a larger series of cases.

Examination revealed that the entire neck of the bladder, including the trigon, was absent. The vaginal wall was rigid as a result of scar tissue. There were total incontinence of urine and partial incontinence of the anal sphincters. A complete successful repair of the perineum was performed by using silkworm sutures. One month later, following complete healing of the perineum and after satisfactory control of the anal sphincters had been demonstrated, the ureters were transplanted to the sigmoid flexure at different times. The wounds healed, and when the patient was dismissed from the clinic one month later, she was passing all urine through the bowel and was entirely comfortable. Follow-up letters reveal that at the present time she passes urine through the rectum about every four hours.

CASE 2.—A woman, aged twenty years, complained of urinary incontinence which had existed since the delivery of her first child four years before she came to the clinic. Three attempts which had been made to close a huge vesicovaginal fistula had been unsuccessful and had resulted in a tremendous amount of scar tissue. The vaginal canal was extensively inflamed from the passage of urine. Physical examination did not reveal any other abnormality. The perineum and anal sphincters were normal.

Examination under anesthesia, on Aug. 21, 1933, revealed that there was complete destruction of the urethra and trigon of the bladder. Bilateral transplantation of the ureters was performed. The right ureter was transplanted Sept. 10, 1933, and the left one was transplanted two weeks later. The wounds healed nicely, and when the patient was dismissed from the clinic one month later, she was passing all of the urine through the rectum.

CASE 3.—A woman, aged thirty-two years, came to the clinic, April 13, 1926, complaining of urinary incontinence which had followed the use of radium for carcinoma of the uterine cervix. She had felt well following the treatment, but two months later she had begun to lose control of micturition and since that time she had been confined to her bed constantly because of complete urinary incontinence.

Examination disclosed a large vesicovaginal fistula and considerable induration in the pelvis. The value for the blood urea was within normal limits and the Wassermann reaction on the blood was negative. The value for the hemoglobin was 65 per cent and there were 3,990,000 erythrocytes in each cubic millimeter of blood. There was no evidence of infection of the upper part of the urinary tract.

Examination under anesthesia did not reveal any malignant change in the pelvis. On April 19, 1927, the right ureter was transplanted to the sigmoid flexure. One month later, the left ureter was exposed and found to be somewhat obstructed and dilated. However, it was transplanted to the sigmoid flexure with a great deal of difficulty on account of the fixation of the bowel at this point. Although the patient passed adequate amounts of urine by the bowel, peritonitis developed; this was complicated by bronchopneumonia and the patient died eight days following transplantation of the left ureter.

CASE 4.—A woman, aged thirty years, came to the clinic Dec. 6, 1926, because she passed all of her urine through the vagina. Following the birth of her child, eight years before she came to the clinic, a high amputation of the cervix had been performed; this had resulted in a vesicovaginal fistula. Three attempts had been made to repair the fistula but none of these had been successful. A suprapubic cystostomy also had been done in an attempt to divert the urine from the vagina. The three attempts at transvesical closure of the fistula had resulted in the formation of scar tissue. Two months after the last attempt to repair the fistula, the scar tissue produced evidence of ureteral obstruction, with repeated chills and fever.

The value for the hemoglobin was 66 per cent and there were 3,700,000 erythrocytes in each cubic millimeter of blood. The Wassermann reaction on the blood was negative and the value for the blood urea was within normal limits. Examination re-

Care must be used not to implant more than 2 cm. of the ureter and not to suture too snugly around its entrance into the wall of the bowel. The line of implantation is then brought laterally to the pelvic wall and the bowel is sutured to the parietal peritoneum by a few interrupted sutures just above the line of anastomosis, thereby relieving any tension on the ureter and adequately protecting against leakage and infection. The left ureter is transplanted in the same manner but not earlier than two weeks after transplantation of the right ureter. Inguinal incisions are used and these are carried through both the external and internal oblique muscles.

VESICOVAGINAL FISTULAS

The urinary bladder obviously is the best receptacle for urine that can be devised; therefore, every effort should be made to save it. Reconstruction of the base of the bladder and vesical neck following their destruction by childbirth has the greatest chance of success at the first operation, so that at this particular time great care should be exercised to get accurate approximation of the tissues. The chances of success in the repair of large vesicovaginal fistulas decrease with each subsequent operation. It is not uncommon to see cases in which repair of a vesicovaginal fistula has been attempted eight to twelve times. This results in scar tissue which makes the anterior wall of the bladder rigid as far as the urethra; urine continues to drain from the fistula and there is little hope of successful repair.

The reason that failure is so likely to occur following repeated operations is that scar tissue has very poor blood supply. In such cases one cannot satisfactorily separate the muscular wall of the bladder from the vaginal wall without risk of further necrosis or the possible occurrence of a fistula that is larger than the one which was present before the operation.

Vesicovaginal fistulas that occur following the treatment of cervical carcinoma with radium are equally as difficult, if not more difficult, to close than are those that occur following delivery. If these fistulas are small the fistulous tracts can be excised and good vesical tissue can be used for closure, but if the fistulas are large, it is almost impossible to reconstruct the bladder and anterior vaginal wall successfully.

CASE 1.—A woman, aged nineteen years, came to the clinic because of a huge vesicovaginal fistula and an extensive third degree laceration of the perineum, which had followed difficult labor. Multiple operations had been performed on both the vesicovaginal fistula and perineum, with only partial success. All urine was passed through the fistula. The upper part of the urinary tract was free from infection and obstruction.

of the bladder. Many of these patients can be kept comfortable by these methods while others cannot. The disease lasts many years and if not held in check the disease process gradually involves more and more of the vesical wall and finally produces a contracted rigid bladder which has a capacity of only a few ounces. This results in frequent micturition, extreme pain, and great disability. The bladder in this state is useless and the urine must be diverted if the patient is to continue to live.

Sebening, of Germany, in experiments on dogs, successfully engrafted a loop of small intestine on to the dome of the bladder and thereby increased the capacity of the latter organ. He then successfully applied this method to the treatment of patients whose bladders had been contracted by infection. The procedure involves considerable risk and for this reason I favor transplantation of the ureters to the pelvic portion of the colon if the rectal sphincter is functioning.

CASE 7.—A woman, aged twenty-seven years, first came to the clinic July 19, 1928, because of pain in the lower part of the abdomen, in the region of the bladder. General physical examination did not reveal any abnormality. Cystoscopic examination revealed a panmural fibrosis. This was treated by transurethral fulguration. Tonsillectomy was performed to eliminate possible foci of infection. Following the fulguration she was free from pain in the region of the bladder for the first time in five or six years. She returned home and was completely free from symptoms for nine months and then had a recurrence of the former trouble.

She returned to the clinic and was treated by overdistention of the bladder to a capacity of 830 c.c. There was slight improvement in her condition for approximately two months but at no time was she completely relieved. A presacral resection of the sympathetic nerve was performed. This procedure afforded considerable relief for one year, but at the end of this time the symptoms recurred. A resection of the involved portion of the bladder was carried out and about a fifth of the bladder was removed. This was followed by considerable subjective relief. However, two years later, following a severe infection of the throat, mild vesical symptoms recurred. Local treatments were carried out for one year but did not produce any improvement.

The right ureter was transplanted to the sigmoid flexure on June 5, 1934, and six weeks later the left ureter was transplanted. The patient returned to the clinic one year following the last operation; she had gained twenty-five pounds (11.3 kg.) and was able to retain the urine in the rectum from four to five hours without distress. Pyelograms of both kidneys were normal.

Comment.—It should be noted that this patient had symptoms for approximately fifteen years before complete relief was obtained by transplantation of the ureters.

CASE 8.—A woman, aged forty-six years, first came to the clinic in November, 1931, complaining of bladder trouble which had existed for six years. Frequent micturition, dysuria, and cramps in the lower part of the abdomen were the chief symptoms. General physical examination did not reveal any other abnormality.

Cystoscopic examination revealed that the bladder had a capacity of only 50 c.c. and that the patient had a severe interstitial cystitis. The bladder was overdistended to a capacity of 250 c.c. There was bleeding from multiple areas of the bladder. The

vealed an extensive scarring in the vagina and a vesicovaginal fistula. The capacity of the bladder was tremendously reduced and the prospects of closure of the fistula and relief of obstruction of the ureter were very poor. The right ureter was transplanted on Dec. 21, 1926, and the left ureter was transplanted on Jan. 13, 1927. The patient has remained in good health and has voided urine through the bowel every three to four hours without discomfort.

CASE 5.—A woman, aged forty-eight years, came to the clinic Jan. 10, 1928, complaining of a rectovaginal and vesicovaginal fistula. Four or five attempts had been made to repair the fistulas but all of these had resulted in failure. Vaginal examination revealed a tremendous scarring in the region of the urethra and a vesicovaginal fistula. Proctoscopic examination disclosed tremendous scarring of the anterior rectal wall and a rectovaginal fistula. Successful closure of the vesicovaginal fistula did not seem probable. Repair of the rectovaginal fistula was carried out on Jan. 23, 1928. A year and a half later, Aug. 9, 1929, the right ureter was transplanted to the sigmoid flexure and a month later the left ureter was transplanted to the sigmoid flexure without incident. The patient's convalescence was uneventful and she passed urine by bowel satisfactorily. The patient died of a pulmonary embolism sixteen days following the last operation.

CASE 6.—A woman, aged thirty years, registered at the clinic Oct. 22, 1928, complaining of a large vesicovaginal fistula which had been present for two years. This had occurred at delivery, which had been spontaneous. Delivery had been followed by phlebitis of the left leg. Six months prior to her admission to the clinic a repair of the vesical fistula had been attempted, but had not been successful. Urinary leakage had increased following this surgical procedure and chills and fever had developed and had continued for several days.

Examination revealed that the blood pressure was normal. The value for the hemoglobin was 48 per cent; there were 3,750,000 erythrocytes in each cubic millimeter of blood and the Wassermann reaction on the blood was normal. Urinalysis did not reveal any abnormality. Vaginal examination revealed a large vesicovaginal fistula. Although prospects of cure of the fistula were poor, it was thought advisable to attempt closure. On Nov. 1, 1928, operation was performed and a very large fistula, which involved practically the entire trigon and extended down to the uterine cervix, was encountered. There was a great deal of scar tissue and the fistula was very difficult to close. Closure was obtained by turning the bladder in with two double rows of sutures of chromic catgut and approximating the vaginal mucous membrane with six silkworm sutures. The capacity of the bladder was very small; therefore, a suprapubic tube was inserted in order to protect the suture line. However, sloughing of the repaired tissues occurred. The right ureter was transplanted to the sigmoid flexure on April 30, 1929, and the left ureter was transplanted on May 24, 1929. These operations were without incident. The patient was in good health following these operations and voided through the rectum every four to five hours.

CHRONIC INTERSTITIAL CYSTITIS

This is one of the most distressing conditions which involves the urinary bladder. A small portion of the bladder may be involved but cases which give one the most trouble are those in which large portions of the bladder are involved. Early in the disease, when only a small portion of the bladder is involved, the involved regions are treated by transurethral applications of silver nitrate, by the cautery, by lavage with numerous medical agents, and finally by overdistention

with instillations of a brand of mild silver-protein (argyrol). The pain had persisted intermittently throughout the treatment but the patient never had passed any blood. Five years before she came to the clinic her bladder had been opened and the ulcerated portion had been excised, but this had failed to relieve the symptoms.

General physical examination at the clinic did not reveal any abnormality. Cystoscopic examination revealed that the upper part of the urinary tract was normal. The capacity of the bladder had been reduced to 120 c.c. There were several linear portions of the vesical wall which contained dilated vessels that were suggestive of interstitial cystitis. The bladder could not be distended beyond a capacity of 350 c.c. Because of the persistence of the symptoms and the reduction in the capacity of the bladder, the right ureter was transplanted to the sigmoid flexure on September 11, 1935, and the left ureter was transplanted on October 3. The patient has been seen recently, approximately one year after her last operation, and has been entirely relieved of her symptoms.

CARCINOMA OF THE BLADDER

This disease occurs much less frequently among women than among men, the ratio of women to men being about 1:5. With the present methods of treatment, effective as they are, it is not often that transplantation of the ureters to the pelvic portion of the colon and total cystectomy are advisable in the treatment of carcinoma of the bladder. With the present scheme of treatment there are two methods of approach: the transurethral and the suprapubic. All pedunculate and small infiltrating lesions which have a low grade of malignancy can be satisfactorily treated by transurethral fulguration. With improvement in the technic some large lesions which have a low grade of malignancy and some small lesions which have a high grade of malignancy may be safely treated by this method. It is usually true, however, that infiltrating lesions which are of large size and have a low grade of malignancy, and practically all lesions which have a high grade of malignancy are more adequately treated by the suprapubic approach. With this approach, one of several methods of treatment may be utilized, such as transvesical electrocoagulation, excision, segmental resection with or without reimplantation of the ureter and radium.

Statistics at the clinic show that the average duration of symptoms in cases of carcinoma of the bladder before patients seek medical care is two years. Furthermore, it is shown that in 25 per cent of cases the lesions are totally inoperable at the time the patients are first examined, and that in this group of cases, treatment of any kind is not advisable. In some of these cases in which there are extensive lesions that are confined to the bladder, or in which there is extensive involvement of the urethra, trigon and ureteral orifices without obstruction and infection of the upper portion of the urinary tract, the patients are perhaps more wisely treated by transplantation of the ureters to the pelvic portion of the colon and by total cystectomy.

patient returned to the clinic one year later for overdistention of the bladder. At this time the bladder was overdistended to a capacity of 300 c.c. with some bleeding. The patient again returned to the clinic in September, 1935, but her condition had not improved. The right ureter was transplanted to the sigmoid flexure on October 1. The patient wished to go home for a few months before transplantation of the left ureter. The left ureter was transplanted on August 7, 1936.

CASE 9.—A woman, aged forty-three years, came to the clinic Sept. 21, 1929, complaining of bladder trouble, which had begun fifteen years previously. She complained of urinary frequency and nocturia, but there was no hematuria. She had had a great deal of treatment for her bladder; this had included fulguration, which at first had produced some relief. Micturition had occurred every ten to fifteen minutes during the night and sometimes had required hypodermics for relief.

General physical examination did not reveal any abnormality. The value for the blood urea was normal; the Wassermann reaction on the blood was negative, and cultures from the right and left ureters did not disclose any evidence of infection. Cystoscopic examination revealed a chronic interstitial cystitis, Grade 3, which apparently involved most of the vesical wall and produced extreme irritability. The capacity of the bladder was only 100 c.c. On account of the greatly reduced capacity of the bladder, and because of failure of the condition to respond to frequent fulgurations, transplantation of the ureters was carried out. The right ureter was transplanted on Sept. 30, 1929, and the left one was transplanted on October 10 of the same year. The patient has remained comfortable and free from vesical symptoms; she is able to retain urine in the bowel from three to five hours.

CASE 10.—A woman, aged fifty-three years, registered at the clinic on April 23, 1935, complaining of pain in the bladder, dysuria, and urinary frequency which had begun ten years previously and had gradually increased in severity. Eight years before she came to the clinic, the uterine cervix had been amputated and a perineorrhaphy had been performed. The bladder also had been irrigated frequently and the right and left ureters had been drained repeatedly, without benefit. A few months after the operation a left salpingectomy, left oophorectomy and appendectomy had been performed, without benefit. Subsequently, several cystoscopic examinations and repeated drainage of the left kidney for a kinked ureter had been performed without improvement. A few months later, a small tumor had been removed from the urinary bladder; the last operation had been followed by an increase in the severity of all the vesical symptoms. For a few months before she came to the clinic she had been taking 3 to 4 gr. (0.2 to 0.24 gm.) of codeine hypodermically, each day, for relief of pain.

Cystoscopic examination revealed that both kidneys and both ureters were normal, and that there was no evidence of stasis. There was interstitial cystitis which was confined largely to the dome of the bladder. The capacity of the bladder was reduced to approximately 100 c.c. The right ureter was transplanted to the sigmoid flexure on April 30, 1935, and the left ureter was transplanted on May 24, 1935, without incident. The patient was dismissed from the hospital about six weeks later. Her general condition was excellent and she was able to retain urine in the bowel for about three hours.

CASE 11.—A woman, aged fifty-three years, first came to the clinic Sept. 4, 1935, complaining of suprapubic pain, loss of fifty pounds (22.7 kg.) in eleven months, loss of strength, dysuria, nocturia and urinary frequency, which had existed seven to eight years but had increased in intensity. She had undergone a myomectomy and perineal repair five or six years prior to her registration at the clinic but these procedures had not produced any benefit. Cystoscopic examination, which had been performed a few months later, had revealed a Hunner's ulcer of the bladder. This had been fulgurized every other week for three years. The ulcer also had been treated

the only chance for the patients in these cases to survive is for the surgeon to eliminate the bladder and transplant the ureters to the pelvic portion of the colon.

The question then is one of rehabilitation from an unendurable state to one of comfortable existence, with a minimal surgical risk. In order to do this, several factors must be considered, namely, the general physical condition of the patient, whether there is any obstruction or infection of the upper part of the urinary tract, the function of both kidneys, the presence or absence of pelvic cellulitis which involves the lower end of the ureters, previous surgical procedures on the pelvis which may have resulted in fixation of the pelvic portion of the colon, and the preparation of the patient for a colonic operation.

Patients who have had total urinary incontinence for several years and who have previously been subjected to unsuccessful surgical procedures for its correction are usually debilitated and discouraged. Most of these patients are anemic and have lost considerable weight, two factors which definitely increase the surgical risk. It is known that postoperative thrombosis and embolism are likely to develop in cases in which the value for the hemoglobin is low and the number of erythrocytes is decreased. The convalescence of those who have lost an appreciable amount of weight is definitely prolonged and they are less able to withstand postoperative respiratory or urinary infections than are those patients who have not lost weight.

Fortunately, in cases of chronic interstitial cystitis, the infection usually remains confined to the bladder and rarely involves the upper portion of the urinary tract unless there are incrustations and fibrosis at the ureteral orifices which produce partial obstruction of either ureter. If the ureter is partially obstructed, ureterectasis, pyelectasis, thickening of the ureter, and infection rapidly supervene. Experience has shown that one assumes a great risk when one transplants a ureter of this type. This is adequately shown in Case 3, in which the patient succumbed to peritonitis and pneumonia. In such instances, if the ureters are known to be thickened and partially obstructed, I believe that it is wise to perform bilateral nephrostomy first and several weeks later, when the infection has subsided, the ureters can be transplanted with considerably less risk. This ureteral complication is most likely to be encountered in dealing with vesicovaginal fistulas which have occurred subsequent to the treatment of carcinoma of the uterine cervix with radium. Pelvic cellulitis frequently is an associated lesion in such instances.

Patients who have carcinoma, especially carcinoma of the urinary bladder, are always considered poor surgical risks. Their tissues heal poorly and it is advisable, whenever possible, to operate on them early, that is, before the carcinoma involves one or both ureters or invades the perivesical fat.

CASE 12.—A woman, aged fifty-two years, who came to the clinic Sept. 10, 1935, had been in excellent health until April, 1935. At this time she had begun to notice moderate pain, urinary smarting and frequency; in July she had passed blood in her urine. Cystoscopic examination had revealed a tumor of the bladder.

Cystoscopic examination revealed an ulcerative neoplasm which involved the right lateral wall and the base of the bladder, adjacent to the internal urethral sphincter, and which extended into the bladder from a position which corresponded to six to eleven on the dial of a clock. Biopsy showed that the tumor was a squamous cell epithelioma, Grade 4. On account of the position of the tumor and the degree of malignancy, bilateral transplantation of the ureters and total cystectomy were performed. The right ureter was transplanted on September 19, and the left ureter was transplanted on October 18. Total cystectomy was performed on November 12. One large lymph node in the right broad ligament was involved. Convalescence was uneventful and when the patient was dismissed from the hospital one month later, all incisions were healed. The patient has remained entirely well to date.

CASE 13.—A woman, aged forty-eight years, came to the clinic Aug. 3, 1929, because of bladder trouble, which had been present for the past five years. Her chief symptoms were urinary burning and frequency, nocturia, and occasional hematuria. She had received a great deal of local treatment, such as irrigations, injections of a brand of mild silver-protein (argyrol), mercurochrome, and had been subjected to several cystoscopic examinations in the three or four years before she came to the clinic.

The values for the blood pressure and blood urea were within normal limits. The Wassermann reaction on the blood was negative. The erythrocyte and leucocyte count, as well as estimations of hemoglobin, gave normal results but the urine contained pus and blood. Cystoscopic examination revealed an ulcerative cystitis and marked irritability of the bladder. While the patient was under anesthesia, the bladder was distended to a capacity of 300 c.c. Biopsy revealed a squamous cell epithelioma, Grade 3, on the anterior and left lateral walls of the bladder. The cystoscopic examination of the bladder revealed other minute malignant areas in the ulcerated mucosa. On account of the ulcerative cystitis, the scattered involvement which had a high degree of malignancy, and the markedly reduced capacity of the bladder, the right ureter was transplanted to the sigmoid flexure on August 16, and the left ureter was transplanted on September 10, and total cystectomy was performed on Oct. 11, 1929, without incident. The patient died of bronchopneumonia on the twelfth day following total cystectomy.

COMMENT

The issue which the surgeon must face in giving relief to patients in such cases is a critical one. Those patients who have complete incontinence of urine as a result of vesicovaginal fistulas not only isolate themselves from society on account of the constant odor of urine, but they become totally disabled from the constant irritation and ulceration of the vulva, perineum and vagina which result from the irritating urine. Those patients who have chronic interstitial cystitis suffer intensely for years from urinary frequency, dysuria and pain in the lower part of the abdomen. The condition is progressive and ultimately terminates in a contracted bladder whose function is practically destroyed. The fact that total cystectomy is advisable in certain cases of carcinoma of the bladder is sufficient evidence that

to postpone transplantation of the second ureter several months if the patient was previously in poor condition. Following transplantation of the first ureter, the symptoms usually are reduced 50 per cent and there usually is rapid improvement in the general condition of the patient.



Fig. 2.—Intravenous urogram, twenty-minute film, made three weeks after transplantation of left ureter to the sigmoid, Aug. 6, 1934. Dilatation, Grade 2 to 3, of pelvis and calices. The right renal pelvis and calices have nearly returned to normal.

The introduction of intravenous urography has been beneficial in the study of the excretory function of the kidneys before and after transplantation of the ureters. Pyelectasis and sometimes ureterectasis can be demonstrated definitely before surgical intervention. This

The problem as to whether one ureter should be transplanted at a time or both ureters transplanted simultaneously is constantly discussed. It is our experience at the clinic that in cases in which the patients are poor, operative risks the risk is increased if both ureters are transplanted to the sigmoid flexure at the same operation. The

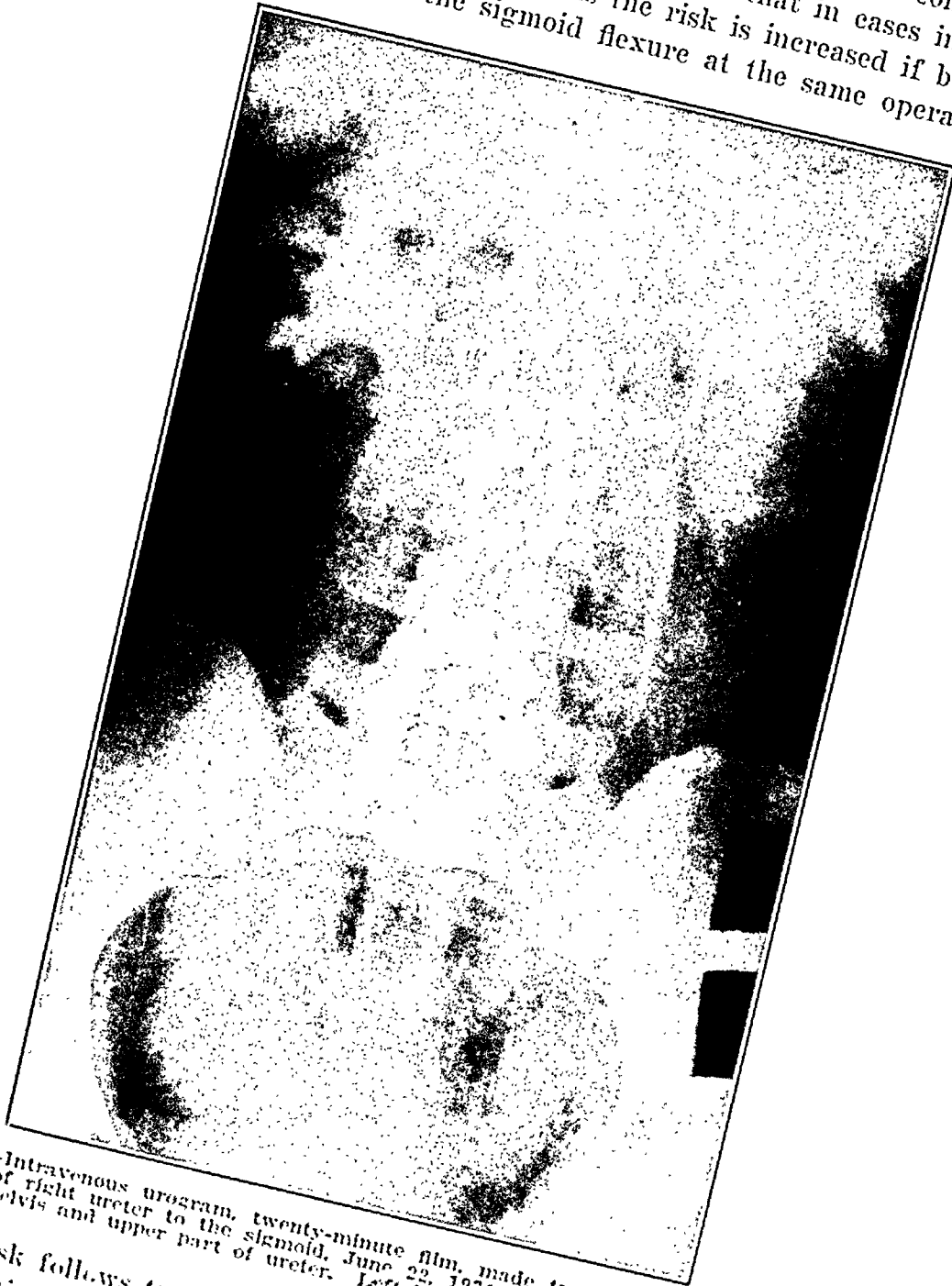


Fig. 1.—Intravenous urogram, twenty-minute film, made two weeks after transplantation of right ureter to the sigmoid, June 22, 1931. Dilatation, Grade 2 to 3, of calices, pelvis and upper part of ureter. Left kidney and ureter normal.

greatest risk follows transplantation of the ureter at the first operation; if patients survive the first operation they usually survive the second one unless the other ureter is diseased. If the Mayo-Coffey technic is used the operation can be done without much trauma and can be completed in thirty to forty minutes. It is frequently advisable

were still dilated, Grade 2 to 3, seventeen days postoperatively (Fig. 3) whereas it is entirely normal after ten months in the five-minute film (Fig. 4).

Cystectomy should be performed following successful transplantation of the ureters in cases of carcinoma of the bladder, but it should

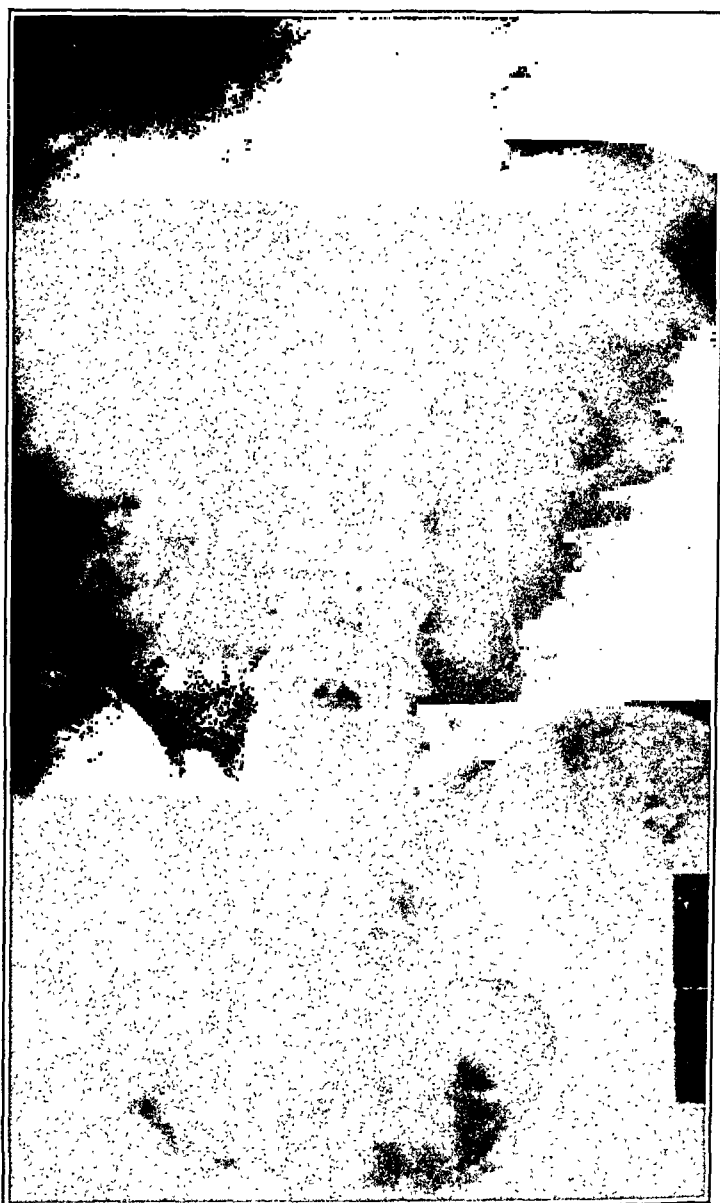


Fig. 4.—Intravenous urogram (same case as Fig. 3) made ten months after transplantation of right ureter to sigmoid, Aug. 6, 1936. Pelvis and ureter normal. Good visualization in five minutes when normal function had returned.

be deferred until both kidneys show evidence of a return of normal function, unless this interval of time endangers successful removal of the bladder because of invasion or extension of the malignancy. I have not found it necessary in any instance so far to perform a cystectomy in a woman who had interstitial cystitis or a vesicovaginal fistula.

method has demonstrated that immediately following transplantation of the ureter there is a dilatation of both the ureter and the renal pelvis; this dilatation lasts approximately two weeks and renal pelvis and ureter return to normal limits if the anastomosis is functioning as it should (Figs. 1 and 2). This is a very definite reason why the



Fig. 3.—Intravenous urogram, sixty-minute film, made seventeen days following transplantation of right ureter to sigmoid, Nov. 12, 1935. Pelvis dilated Grade 2, calices dilated Grade 3, upper third of ureter dilated Grade 2.

ureter should not be transplanted until an intravenous urogram has proved that the other ureter and kidney have returned to normal limits. Not infrequently, this return of function may be prolonged for several days or weeks because of edema or infection which occurs at the time of anastomosis. Such a condition occurred in Case 8. The intravenous urogram revealed that the renal pelvis, calices, and ureter

The preparation of the patient for operation for ureterosigmoidal transplantation is just as essential as it is for other operations on the large bowel.

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ABSTRACT OF DISCUSSION

DR. W. W. BABCOCK, PHILADELPHIA, PA.—Dr. Counsellor has had in 13 cases a hospital mortality from various causes of 23 per cent. Despite the early renal reactions, in none of the surviving patients was there found evidence of serious late damage to the kidneys. Of course, I do not believe that Dr. Counsellor will contend that none of these patients in later life will lose a kidney from ascending infection or that some will not die from this cause. However, by technical improvements in the operation the danger has been much reduced.

The transplantation of the ureters from the exstrophic bladder to the rectum or sigmoid certainly warrants the risk incurred. The old operation of Maydl, now neglected, in which an island of bladder containing the ureters is turned over and implanted in the underlying rectum, is a very good one, particularly as the ureteral sphincters are retained. The operation, which is not difficult, unfortunately is not feasible except in exstrophy. In those rare patients who require a cystectomy for cancer of the bladder, certainly the method described by Dr. Counsellor is the one to be considered, as it also is in certain obstructions of the ureters where drainage into the urinary tract is not feasible.

Dr. Counsellor reports six ureteral transplantations for vesicovaginal fistula, and as two patients died after the operation, the mortality was 33 per cent. When we have a mortality of 33 per cent from operating upon a condition which of itself does not destroy life, we should of course look for a safer method of treatment. Doubtless many of these patients would prefer to wear a ball or other occluding pessary or a urinal rather than take such a risk. In the vesicovaginal fistulas we often forget that Marion Sims discovered that silver wire sutures were essential for successful closure. Fortunately we now have wire that is softer, stronger, even less irritating than the silver wire used by Sims. Annealed alloy steel wire ties well in an ordinary square or surgeon's knot, may be procured as fine as a hair and when left in the bladder or ureter, apparently it does not become encrusted.

Catgut should in my opinion never be used even as a ligature in these operations. The bladder wall must be thoroughly liberated, for even if very small the bladder after closure will gradually dilate under use. It is not necessary to turn the patient upon her face after the operation, nor to do a suprapubic drainage, nor to operate through the abdomen. Thus far, I have seen no vesicovaginal fistula not due to malignant disease that could not be closed by following the methods discovered by Sims, and, of course, the operation is practically without mortality.

DR. COUNSELLER (closing).—If one considers the mortality of each separate group, it does show a very high percentage for vesicovaginal fistulas, but the 13 cases should really be considered as a single group in which transplantation of the ureters has been performed. The two deaths in the vesicovaginal fistula division were attributable to pulmonary embolism in one case, and to pneumonia in the second. Pneumonia, of course, is a very serious hazard to patients who are greatly devitalized by the condition for which they seek treatment.

The bladder should be irrigated once daily while the patient is in the hospital, and once a week for six weeks thereafter. The infection apparently subsides and causes no further trouble following diversion of the urine.

The preparation of the colon and peritoneal cavity is, I feel, one of the most important steps in the insurance of a successful result in these cases. The preparation is identical with that used in dealing with lesions of the large intestine in cases in which resection is considered.

All patients are hospitalized three to four days before operation. During this period an effort is made to cleanse the bowel as thoroughly as possible without increasing the debility of the patient. This usually can be accomplished satisfactorily by giving a diet high in carbohydrates and by the use of mild saline cathartics.

In addition to preparation of the intestine, vaccine is administered intraperitoneally forty-eight to sixty hours prior to operation, as a preventive against peritonitis. In the past seven years at the clinic, Dixon and his colleagues on the colonic service have administered vaccine intraperitoneally to 2,500 patients previous to the performance of some type of intestinal operation, and during this period the mortality from peritonitis following intestinal operations has decreased 66 per cent. On account of these good results, the same preoperative preparation has been adopted for ureterosigmoidal anastomosis.

SUMMARY

Transplantation of the ureters of women to the sigmoid flexure is a sound surgical procedure for the treatment of huge vesicovaginal fistulas, chronic interstitial cystitis with secondary contraction of the bladder in cases in which the bladder has been rendered useless, and some carcinomas of the bladder.

Thirteen illustrative cases have been briefly described. There were three deaths; one from peritonitis and bronchopneumonia, one from pulmonary embolism, and one from bronchopneumonia alone. In the one case in which the patient died of peritonitis and bronchopneumonia, death followed transplantation of a badly diseased ureter after previous transplantation of the opposite ureter; peritonitis developed because there was an infection of the upper portion of the urinary tract. The operative risk is decreased when one ureter is transplanted at a time.

Introduction of intravenous urography has been beneficial in the study of the excretory function of the kidneys before and after transplantation of the ureters. It also aids in determining the degree of pyelectasis and ureterectasis following transplantation, and the return of the renal pelvis and ureter to normal several weeks or months later.

while in 3 of these 4 cases fluid was also present in the chest. Lynch states that in Petersen's collected series of 84 cases ascites was present in 40 per cent. Hoon's report shows that 25 per cent of 55 cases were accompanied by ascites and 2 of the 55 had chest fluid. It is rare, however, to find textbooks that mention fluid in the chest. Frank,* in reviewing Stoeckel's *Handbuch der Gynäkologie*, states that "in dealing with fibroma of the ovary, no mention of the occurrence and frequency of hydrothorax is given, although this is now a well-recognized syndrome in combination with ascites.*" It is our belief, however, that the occurrence is not well recognized and that general knowledge of the fact is almost everywhere lacking.

SYMPTOMS

The ages and marital states of the patients in this group are charted below. No young and no really old person is included among the patients, and neither sterility nor fertility seemed to play a part (Table I).

TABLE I

CASE NO.	AGE	CHILDREN
1 (single)	42	0
2 (married)	55	1
3 (married)	38	2
4 (married)	36	1
5 (married)	53	0
6 (?)	64	?
7 (single)	52	0

The predominating symptoms were those of interference with proper aeration. In all cases dyspnea, pain, and discomfort in the chest were present. Some of the patients had had chest taps done some time previous to their admission, and in one patient (Case 5) pleurisy had been diagnosed five years before entry. The next most important symptom was "bloating"; 4 of the 7 patients noticed an increase in size of their abdomen with accompanying discomfort. Upset menstrual periods were not uncommon, and both amenorrhea and metrorrhagia were present in 3 cases.

PHYSICAL EXAMINATION

Physical examination disclosed the presence of fluid in the chest in every case, and in the abdomen in 6. A mass was detected in the abdomen or pelvis in 6. Two patients were definitely below par and undernourished, whereas 3 others were stated to be well developed and nourished, and 1 was apparently quite ill at the time of her examination. Fluid was found in the right chest in 5 instances, in the left in 1, and in both in 1.

*NOTE.—Dr. Frank refers to an article in the *Journal of the Mount Sinai Hospital*, November-December, 1934, by U. J. Salmon. In this paper one case of fibroma of the ovary with ascites and hydrothorax is described. It seems to be the same type of lesion with the same findings as described in our paper. Two other cases are reported; one a patient with a fibroid with fluid in the abdomen and chest, and one other with a fibroid with fluid in the abdomen. Salmon's case is the second report that has been found in a search through the literature.

I am thoroughly familiar with the work of Marion Sims, but I do not believe that the silver wire can be utilized in the type of cases I am discussing here. These are cases in which the capacity of the bladder has been reduced very greatly, and in certain instances the vesical neck and urethra have been completely destroyed.

In some cases the perineum has likewise been destroyed, and in these it is necessary first to reconstruct the anterior rectal wall, perineum, and sphincter. Later one ureter and then the other can be transplanted without much risk if there is no pelvic cellulitis or infection of the ureter.

Dr. Babcock is quite right in stating that the use of excessive catgut in repair predisposes to fistula. Furthermore, it is correct that when it can be repaired from below, the bladder must be mobilized and good tissue obtained. This brings up again the point that in most of these cases the vaginal wall has been so destroyed that such tissue cannot be obtained to close over the bladder.

FIBROMA OF THE OVARY WITH ASCITES AND HYDROTHORAX*

WITH A REPORT OF SEVEN CASES

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INTRODUCTION

IT HAS long been known that fibromas of the ovary are accompanied by fluid in the abdomen. In a review of the literature for the past twenty-five years but one case report of a patient with fluid in the chest as well as in the abdomen was uncovered. In a paper by Hoon of the Mayo Clinic two cases are mentioned, and in a review of all the ovarian tumors at the Massachusetts General Hospital three cases were found and mentioned in *Tumors of the Female Pelvic Organs*, by Meigs. It was the intention of one of the authors (Meigs) to report these three cases in detail, but another patient entered the hospital in 1934 under charge of one of us (Cass) and was operated upon by L. S. McKittrick, making four; the courtesy of the Mayo Clinic in allowing the use of the complete protocols of their two cases, plus the case report by Leo, made a series of seven cases available and thus constituted a much more satisfactory endeavor. It is our belief that this group stands as the largest series reported to date in any literature at any time.

HISTORY

In nearly all textbooks of pathology and gynecology mention is made of the fact that ascites often accompanies fibromas of the ovary. Rarely is the exact percentage given in any group of fibromas studied. However, in the Massachusetts General Hospital series of 29 cases, 4, or 13.7 per cent had accompanying ascites,

*The authors wish to thank the Macmillan Company for their courtesy in allowing them to use the illustrations taken from Meigs, *Tumors of the Female Pelvic Organs*, New York, 1934.

cavity; this changed the innocent transudation into a real empyema. Some patients were tapped before they arrived at the hospital, and in one it was necessary to tap the chest once after operation for removal of the fibroma. Table II shows the number of tappings, chest and abdominal, done upon each patient.

OPERATION

Operation consisted in all instances of an exploratory operation with removal of a hard, solid, fibrous tumor of the ovary. In many instances the outcome was considered very dubious, the tumor at operation being thought a malignant one. "A single ovary was involved in all cases, and in but one was the other ovary and the uterus removed. Fluid was present in all cases from large amounts to six to eight quarts. It was reported as straw-colored, yellow, green yellow, yellow brown, and clear. In four cases adhesions were encountered, but in only one were they severe. The size of the tumor varied, but in all instances it was considerable, from "large" to the size of a child's head or 20 cm. in diameter. In three instances the left ovary was involved and in two the right ovary; in the other two the side affected was not known. Table III gives a graphic picture of the operative findings.

TABLE III

CASE	FLUID	AMOUNT	ADHESIONS	SIZE	POSITION
1	Straw	Considerable	Yes	20 cm.	Ovary
2	Clear	6-8 quarts	Yes	14 cm.	Right ovary
3	Yellow brown	Several quarts	Yes	20 cm.	Left ovary
4	?	Marked	Extreme	Child's head	Ovary
5	Straw	Several liters	Doubtful	Grapefruit	Right ovary
6	Green yellow	Large amount	Doubtful	Large	Left ovary
7	Yellowish	Large amount	Doubtful	Large	Left ovary

There were no fatalities following the operation, and in only one was the convalescence mentioned as difficult. In one case (Case 6) it was necessary to tap the chest on the fifteenth postoperative day, but that tap cleared the chest of fluid permanently.

PATHOLOGY

All tumors were fibromas or fibromyomas of the diffuse type, nearly the whole ovary being involved. Such tumors are described as arising from the stroma, the corpus luteum, the corpus albicans, the theca interna or externa, the tunica, organized blood clots, and even from the walls of blood vessels. It is most probable, however, that such tumors arise from the connective tissue stroma of the ovary. In three instances the tumor was called a fibromyoma because of the presence of suspected muscle fibers. It has long been recognized that certain fibromas con-

The history and physical examination brings out the fact that the fluid could be readily detected in the chest and abdomen and that an accompanying abdominal or pelvic mass was easy to make out. With a knowledge of the possibility of this entity being present it would seem that a diagnosis should have been arrived at without difficulty in most instances.

LABORATORY FINDINGS

The laboratory findings are not so complete as they should have been. The specific gravity of the fluid removed was accurately recorded in but few instances, but in two cases the chest fluid was reported as 1.016 and 1.017. The abdominal fluid in one case was recorded as 1.017 and 1.018. In the other cases the fluid was called typical of a transudate. Usually the specific gravity of chest fluid in a transudate is given as below 1.015 and that of an inflammatory exudate as over 1.018. It is rather difficult to place this fluid as typical of either, but as it was called definitely a transudate after laboratory study on two occasions, it is probably correct without further data to call it that. The fluid removed from 3 patients was "pigged" and in all 3 instances was reported as negative for tuberculosis. In 2 cases skin tuberculin tests were done and 2 tests were reported as positive and 1 as negative. Twice the fluid was cultured and twice it was reported as negative for bacteria. The white blood count varied from 6,000 to 12,000, with no real evidence of a leucocytosis. In no instance was there an elevation of temperature above 99.8°, such as is characteristic of an inflammatory exudate in the chest.

It may be reasonably concluded from the above data that the fluid caused very little systemic reaction, that it probably was of a transudate type rather than an exudate, and that it was not of a tubercular nature.

TREATMENT BEFORE OPERATION

The treatment before operation usually consisted of chest or abdominal paracentesis. It is interesting to observe how many times both chest and abdominal taps were done before it was decided to remove the abdominal tumor, the actual cause of the fluids. Case 1 was tapped four times and at the fourth paracentesis two tubes were placed in the chest

TABLE II

CASE NO.	CHEST	ABDOMEN
1	4	1
2	5	0
3	7	4
4	0	0
5	3	1
6	Repeated	0
7	Repeated	1

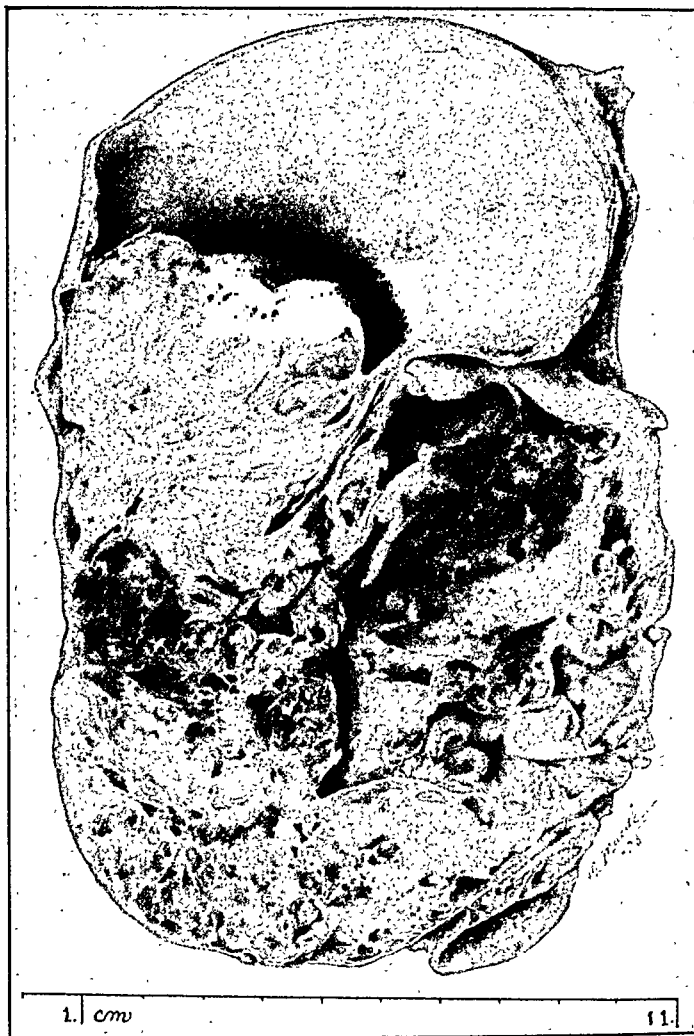


Fig. 2.—Large fibroma of the ovary with marked areas of infarction, necrosis, and cystic changes.

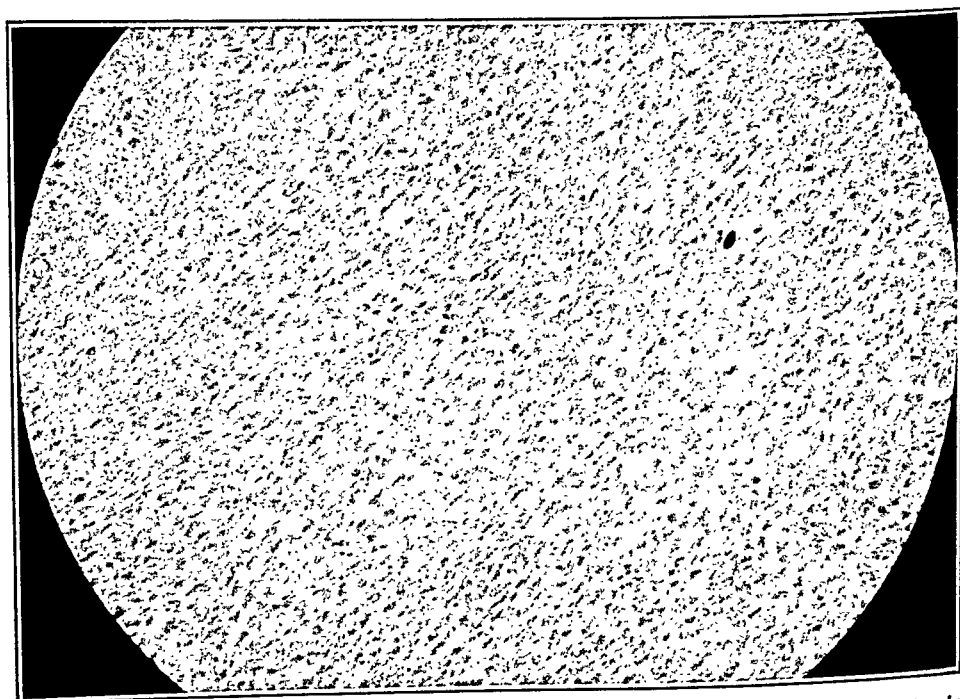


Fig. 3.—Photomicrograph of a cellular fibroma of the ovary. This slide is typical of the histology of such tumors.

tain a small amount of muscle tissue, and without differential staining (not done in these cases) it is very difficult to state whether the tumor is a fibroma or a myoma. From the description of the tumors as given in the pathologic reports, all were of the same type, i.e., large, smooth, and lobulated.

The most common change in such tumors is degeneration, and the formation of cystic and necrotic areas in the tumor bulk. These areas are probably due to circulatory changes produced by poor blood supply



FIG. 1.—Fibroma of the ovary showing the characteristic type of tough, white, fibrous tumor tissue. The cysts may be due to degeneration or to accompanying cystic change in the remaining ovarian tissue.

or to the twisting and untwisting of the tumor on its pedicle with impairment of the blood supply. It does not seem possible that a tumor not entirely infarcted or at least greatly necrotic, and with only small cystic areas and small areas of necrosis, could be responsible for the liters of fluid found in the abdomen. The histology of all tumors was quite typical; interlacing bundles of connective tissue with some areas suspected of being smooth muscle. Both cellular and noncellular types occurred.

the fluid was in the left chest, and in another in both. These facts exclude the possibility of an azygos obstruction at least being the only etiologic factor. From the histories of the patients, the chest fluid appears to cause the first and most important symptoms. In some cases the abdominal fluid was not sufficient to cause any symptoms when the fluid in the chest was embarrassing the patient. If in some way an opening might be found in the chest cavity that would allow free communication with the abdomen, the hydrothorax would be explained, but it is doubtful if there is any such communication. After much discussion with surgeons and pathologists interested in thoracic disease, and with internists, it has been impossible to give any logical etiology that can withstand all criticism.

Below are presented in detail the case histories of the seven cases:

CASE 1.—(Massachusetts General Hospital.) A forty-two-year-old single woman entered the hospital on April 29, 1901, complaining of pain in the right chest of one week's duration. Pain had increased gradually and she had become short of breath. The catamenial history was negative until three years before, when she occasionally skipped a month. Her mother and father had died of consumption; the rest of her family history was negative. Her past history was negative. She had had no cough, dyspnea, or pain before the present illness.

Physical examination showed a well-developed and nourished woman. The heart was negative. There was flatness over the right chest throughout with diminished voice sound and fremitus. Respiration was also much diminished. The left chest was negative. The abdomen showed a large, hard mass extending up to the umbilicus. Several nodules like small fibroids could be felt over it.

On April 30, 1901, 80 ounces of clear fluid were aspirated from the right chest. This made the patient much more comfortable, but physical signs showed that there was still considerable fluid present. On May 3, 1901, 62 ounces were withdrawn with much relief to the patient. (An inoculation from this chest fluid was made in a guinea pig. The animal was found dead on May 21 and an autopsy was performed which showed no evidence of tuberculosis.) The patient made an uninterrupted convalescence and was discharged much relieved on May 7, 1901.

On May 28, 1901, the patient was readmitted, complaining of cough with considerable yellowish sputum without blood. For the past two weeks dyspnea had again steadily progressed, so that she was unable to lie on the left side and could walk only with difficulty. She had had no fever, night sweats, or loss of weight. There had been no chills, anorexia, nausea, or vomiting. She had been unable to work for four weeks.

Physical examination showed both lungs symmetrical with expansion of the left greater than the right. There was right chest flatness below the level of the spine of the scapular and second rib in front with dullness above these limits and tactile fremitus diminished above and absent below. Interspaces were slightly fuller over the right chest. Respiration was feeble and with diminished voice sounds. There was no egophony or increased whisper. No râles were heard with patient sitting up and there was no change with change of position. Heart impulse was palpable in the fifth space in the anterior axillary line and dullness corresponded 15 cm. from the midsternum. The sounds were of good quality and there were no murmurs. Pulses were equal and synchronous, of low tension, small volume, and regular. The liver above was undetermined and the lower limit was one finger below the costal margin by percussion but was not felt. The spleen was not felt. The abdomen was convex both ways, abruptly prominent, and slightly fuller in the right

END-RESULTS

The result in each case was excellent. No deaths followed the operation, and in all instances, as far as followed up, no return of abdominal or chest fluid was noted. In Table IV is shown the length of follow-up in each patient.

TABLE IV

CASE	ENTERED HOSPITAL	OPERATION	FOLLOW-UP
1	April 29, 1901	Sept. 20, 1901	Dec., 1902
2	June 9, 1902	June 10, 1902	Oct. 25, 1913 (died)
3	Oct. 9, 1908	Dec. 12, 1908	Nov. 11, 1935
4	July 31, 1917	Aug. 16, 1917	Sept., 1921
5	Nov. 20, 1920	Dec. 9, 1920	June, 1921
6	March 25, 1926	July 25, 1926	Oct., 1926
7	Aug. 5, 1934	Aug. 18, 1934	Dec., 1935

In two cases the follow-up is not so long as it should be but in the other five a satisfactory end-result has been checked for from one year to twenty-seven.

DISCUSSION

The reason for the presence of fluid in the abdomen and chest in such cases is not clear. The ascites has been ascribed for many years to the irritation of the peritoneum by the hard tumor mass. It is possible that such irritation might cause abdominal fluid, but it does not seem possible to explain fluid in the chest by such reasoning. Both fluids are part of the same process, for removal of the tumor of the ovary caused the chest fluid to disappear also. It might be imagined that fluid from the abdomen could get into the chest cavity by direct extension, but anatomically this does not appear to be possible. The chest cavities are hollow boxes, and if there were any communication with the area below the diaphragm there ought to be some difficulty with the normal process of respiration. If the tumor were malignant and had metastasized to the chest it would be easy to understand the presence of fluid, but no such pathology is present. Ascites can be caused by metastatic tumor with secreting areas in the tumor, such as is present in the papillary cystadenoma of the ovary. It may be due to a general renal or cardiac failure. Inflammatory processes, such as peritonitis and especially tuberculous peritonitis, are often accompanied by abdominal fluid. Portal obstruction is known to cause ascites in certain cirrhoses of the liver. But how to explain the presence of abdominal fluid by a freely movable tumor of the ovary is difficult enough without having to explain the presence of fluid in the chest and its cure by removal of such a tumor. The fluid is probably a transudate, and thus it would seem to be due to some pressure or obstruction, but how a pelvic tumor could cause sufficient pressure to permit the accumulation of quarts of fluid is difficult to explain. Lack of drainage of the right chest by the azygos vein may play a part, but in one case

in places quite cellular, in others less so. Throughout the growth were chinklike spaces which were evidently of vascular origin. A diagnosis of fibromyoma was made.

In December, 1902, the patient wrote that she was in excellent health and had been married the previous September.

CASE 2.—(Massachusetts General Hospital.) A fifty-five-year-old married woman, with one child, entered the hospital on June 9, 1902, stating that seven months previously she had felt something give way in the vagina when she was carrying a basket of clothes. A small mass appeared at the vulva, where it still remained. She had had slight bleeding from the vagina ever since. Five months previously she had had "pleurisy" with a slight cough and pain in the lower chest in front, not especially connected with respiration. She was in bed for three months and had never been strong since. She was tapped five times in the right back and 2 to 4 quarts of fluid were removed. For the past two weeks her abdomen, which had always been prominent, had increased rapidly in size. She was constipated but her bowels moved well with physic. She had occasional vomiting without blood and considerable abdominal discomfort. The family history was negative. There were no neoplasms among her relatives. She had never been ill and had worked hard up to five months before admission. Three years before she had noticed a tumor moving from side to side in the lower abdomen; it moved itself and felt "like a baby." She had no pain or discomfort from this mass.

Physical examination showed a well-developed and poorly nourished woman, with fairly good color. She had a small, rapid pulse of low tension. The heart was negative. Respirations were slightly harsh all over with an occasional r le, especially in the right base. There was dullness in the right axilla and right back below the angle of the scapula with practically no respiration or voice sounds. Liver dullness began at the fifth rib in front. The abdomen was greatly distended, with shifting dullness in flanks and tympany in the upper portion of the abdomen. There was a marked percussion wave. Nothing was palpable through the distended abdominal wall. There was slight dilatation of superficial veins. No edema of legs or face was noted. Pelvic examination showed a polyp, the size of an English walnut, presenting at the vulva with a narrow pedicle springing from the posterior wall of the interior of the cervix. Bimanual examination was unsatisfactory; the uterus appeared to be in good position and not enlarged. The culdesacs were full of fluid. There was slight tenderness in the left culdesac.

At operation on June 10, under ether anesthesia, an incision was made in the median line below the umbilicus. The peritoneum was opened and 6 to 8 quarts of yellow clear fluid escaped. A mass in the right side was brought into the wound and found to be an ovary the size of a coconut. A few adhesions were separated. The ovary and part of the tube were removed. Manual examination of other organs showed them to be apparently normal. On June 26 the patient was discharged well.

The pathologic report showed an irregular lobulated mass covered in most parts by peritoneum. Weight 1 kilogram, 14 cm. in diameter. Adherent to one side was the fallopian tube, 6 cm. long and normal. In one place the omentum, which contained many large vessels, was adherent. On section there were masses of grayish tissue separated by bands of edematous connective tissue. A diagnosis of edematous fibromyoma was made.

The patient died on Oct. 25, 1913, eleven years postoperatively. The cause of death was given as senility and ventral hernia.

CASE 3.—(Massachusetts General Hospital.) A thirty-eight-year-old married woman with two children entered the hospital on Oct. 9, 1908, complaining of not having felt well for the past year. She had had some pain in her shoulders and back. Seven months previously she consulted a physician because of pain in the

lower quadrant. A hard mass could be felt rising from the pelvis to two fingers from the anterior superior spine on the right, thence to two fingers above the navel line and descending to the left; this mass was hard, nontender, nonfluctuant, apparently overlaid by intestines, and movable laterally and anteroposteriorly. The flanks were tympanitic. Vaginal examination showed that the introitus admitted two fingers with difficulty. The cervix was low, of normal size, conical, and pointed perpendicular to axis of the vagina. The same hard mass was felt in the left vault and the posterior culdesac. The body of the uterus could not be made out. Hemoglobin was 85 per cent and the white blood count 11,000. The urine was normal.

On May 29 the patient was uncomfortable from dyspnea all night. The right chest was tapped and 68½ ounces of clear, straw-colored fluid were withdrawn with a specific gravity of 1016, slightly alkaline, and the albumin content was 3.2 per cent. A slight sediment contained mostly fibrin flakes with a few degenerated epithelial cells and leucocytes. No organisms were found.

On June 1 the right chest was again tapped and 58 ounces were withdrawn. The fluid was clear and straw-colored with a specific gravity of 1017, slightly alkaline, albumin 3 per cent.

On June 3 a surgical drainage of the pleurisy with effusion was done under cocaine anesthesia. An incision 2 inches long was made through the skin. A needle was introduced, followed by the escape of yellow fluid. A knife was passed in and an incision made through the intercostal muscles and pleura between the seventh and eighth ribs. Two small tubes were introduced and much fluid escaped (about 48 ounces).

On June 10 the patient spent a rather uncomfortable day. She was not draining so much; the abdominal growth seemed increasing in size, and there was a question of ascitic fluid. She was losing ground a little. On June 12 she had considerable pain and was draining profusely. Her abdomen was tapped and the fluid injected into a guinea pig.

On July 2 the patient had lost strength. Her feet were swollen. Her cavity was washed out every day and 4 ounces of foul pus were withdrawn. There was considerable distention of the abdomen. The abdomen was tapped again on July 7 and over 6 pints of reddish fluid were withdrawn. On Aug. 13, 1901, the patient was discharged much relieved.

On September 18 of the same year the patient reentered the hospital for operation for an abdominal tumor, considered to be fibroid of the uterus. She had improved constantly and gained eight pounds in the two weeks previous to readmission.

Under ether anesthesia an ovarian tumor was removed on September 20. A long median suprapubic incision was made and the peritoneum opened with immediate escape of considerable straw-colored fluid. A large whitish mass was at once found. After some manipulation with the breaking up of adhesions, a mass about the size of a child's head, very solid and whitish in color, was removed. The pedicle, including the tube, was then tied off with stout silk, was clamped, and cut off. The appendix was examined and found to be somewhat enlarged and adherent and it was removed. The wound was closed with silk. On October 19 the patient was discharged well and in good condition.

The pathologic report showed the ovary was an irregularly rounded tumor mass measuring 20 cm. in greatest diameter and weighing 2440 gm. On section the surface was moist, with numerous small cystic cavities, and on one side a remnant of ovarian tissue could be made out. The outer surface was covered with thin, fibrous membrane in which were numerous thin-walled veins and some slight adhesions. The consistency was firm, almost cartilaginous, and at one place the surface was deeply fissured. The tube was normal. Microscopic examination showed the structure to be made up of interlacing masses of fibrous and muscular tissue.

The fluid in the abdomen increased while the fluid in the chest seemed to be less. On October 25 the patient's abdomen was again tapped low down in the right flank and 14 pints and 9 ounces of a clear yellow fluid were obtained. Girth before tapping measured 100 cm. and after tapping 83 cm. Report of the ascitic fluid showed slightly cloudy straw-colored fluid without clot. Reaction was alkaline. Specific gravity was 1017, albumin 2 per cent. Smear showed excess of lymphocytes. Differential count showed lymphocytes 65 per cent, endothelial cells 34 per cent, neutrophils 1 per cent. Bacteriologic report: one colony of *Staphylococcus albus* (considered a contamination).

On October 29 the left chest was tapped; it was thought best to remove only 8 ounces because the fluid had been in the chest so long. Small amounts were to be taken out at intervals so as to encourage expansion of the lung. Report of the chest fluid: pale yellow, straw-colored without clot, specific gravity 1017, albumin 1.7 per cent. Smear of sediment showed a predominance of lymphocytes. Lymphocytes 55 per cent, endothelial cells 44 per cent, polymorphonuclear cells 1 per cent.

On November 3, 8 ounces of fluid were removed from the left chest; there seemed to be no return of fluid after the last tapping. Breathing was easier. Skin tuberculin reaction on November 6 was strongly positive. On November 7 the left chest was again tapped and about 8 ounces of fluid were removed. Immediately afterward the abdomen was tapped in the right flank and 15 pints of fluid were removed. The girth of the abdomen after tapping was 88.5 cm.

On November 10 there was distinct gain over the fluid in the chest. There was resonance to the third rib in front and midscapula behind. Breathing over this area was as good as on the sound side. There was a right border of cardiac dullness 4 cm. to the right of the median line.

The left chest was tapped on November 12 and 8 to 10 ounces of fluid were removed. Ascites increased and was associated with edema of legs. Chest signs remained unchanged. The patient was started on catharsis and diuresis on November 20 to see if ascites would diminish. The girth of the abdomen was 108 cm. The abdomen was tapped on November 21 and 18 pints were obtained. On November 28 the girth of the abdomen had increased to 103.5 cm. and the patient had gained 4 pounds in weight in twenty-four hours. Vaginal examination at this time showed a mass filling the pelvis, crowding the cervix behind the pubes, continuous with the suprapubic tumor. The mass was very hard, irregular, nonelastic and in the median line. Operation was advised to relieve a suspected tuberculous condition of the peritoneum and for diagnosis of the uterine tumor.

On December 5 there was so much discomfort caused from the full abdomen that it was tapped and 260 ounces of fluid were obtained, similar in character to the previous fluids. On December 8 the left chest was tapped and nearly 2 quarts of fluid were obtained. It was hoped that this would give the lung a better chance to expand.

Operation was performed on December 12. A two-inch median incision was made. The peritoneum was opened with a spurt of a thin yellowish brown fluid, several quarts in amount. A solid ovarian tumor was then delivered with some difficulty. The pedicle was clamped and cut and the tumor removed. Gauzes were packed into the pelvis. The pedicle arising from the left broad ligament was tied off with silk and the ovary of that side removed. Several bleeding points due to ruptured adhesions were caught and tied. The abdomen was explored and nothing else abnormal was found.

The pathologic report showed a solid tumor occupying the region of the ovary, measuring about 20 cm. in diameter, flattened, and upon section having a white fibrous surface with some areas slightly hemorrhagic in character. Microscopic

left side, which felt sharp and knifelike and prevented sleep. A left pleural effusion was found, the chest was tapped, and two quarts of fluid were obtained. She had been at rest, had been out of doors, and had had an extra diet with improvement, but the fluid returned very rapidly. About four weeks prior to her admission she had noticed the abdomen increasing in size; this continued up to the time of admission. She had had some dyspnea on exertion for a good many years, but it had been worse since the fluid in the chest appeared and very bad since the fluid in the abdomen had been noticed. She could not lie down flat but could get up the stairs. She had not remained in bed at any time. For two days previous to her admission her feet and legs had been swollen. Her appetite was good. She had occasional vomiting after coughing. Bowels were loose. She had no urinary disturbance. A note from her local physician stated that her urine was normal. Three examinations of the sputum had been negative for tubercle bacilli.

The patient's mother had died suddenly and had had a cough for a long time. There was no history of familial disease. Her periods began at fourteen and were regular and painful. She had had a cough since she was a girl, with a little yellow sputum and no blood. There had been no recent increase. Twelve months previously a doctor had found a uterine fibroid, and for two to three years previously she had felt something wrong in the region of the uterus. She had had no treatment. There had been no ascites.

Physical examination showed a well-developed and nourished woman with skin and mucous membranes of good color. She breathed easily in half-recumbent position or bed rest. No cervical, axillary, or inguinal glands were felt. On examination of the heart apex impulse was not seen or felt, but pulsation was felt best to the right of the sternum. The left border of dullness was not determined. The right border of dullness in the fourth interspace was 6.5 cm. to the right of the midsternum. Sounds were best heard to the right of the sternum. They were regular and of good quality. There were no murmurs. Pulses were synchronous, equal, regular, and of fair volume and tension. The left chest was flat throughout and breathing was distant bronchial. Whispered voice was increased throughout. The spoken voice was distant and at the base behind close to the spine there was egophony. Tactile fremitus was absent. There was dullness of the paravertebral triangle on the right: base of 6 cm., altitude of 5 cm. There was flatness below the fifth rib in the mammary line on the right. The line of flatness extended around the chest in a horizontal line to 2.5 cm. below the lower angle of the scapula in the back. Breathing throughout the right chest was normal. The abdomen was very prominent, the greatest girth being midway between the umbilicus and pubes and measuring 110 cm. The umbilicus was flush. The abdomen was tense but not rigid. No masses could be felt. No tenderness or shifting dullness was noted. A fluid wave was obtained. Liver dullness began at the fifth rib, the lower border not being determined. The edge was not felt. Splenic dullness was not determined and the edge was not felt. There was slight soft edema of the feet and ankles.

On October 10 the patient's abdomen was tapped, 18 pints of clear yellow fluid being obtained, and the end of the trocar came against a solid tumor which somewhat interfered with the flow.

Report of the ascitic fluid showed nine quarts of clear straw-colored fluid, alkaline, specific gravity 1018, albumin 2.4 per cent. A culture was taken and a guinea pig injected. Smears showed a predominance of lymphocytes. Some of the fluid was injected into a guinea pig; the animal was killed on Nov. 14, 1908 and autopsy showed no tuberculosis. On October 19 skin tuberculin was negative after forty-eight hours. The patient complained of abdominal pain radiating to the right chest, nausea, and frequent vomiting. She had no fever and there was no change in physical signs.

and expectoration. She had steadily lost weight and strength, but there was no coughing or expectoration at the time of her admission. During the last month she had noticed some bloody discharge from the womb, between menstrual periods.

The family history contained no evidence of cancer or tuberculosis. The patient's first menstrual period, at the age of twelve, had been very painful and since then the periods had been regular. The patient had had a child at the age of thirty-two, at which time labor had been very difficult. Forceps had been used and there was a bad tear from labor. The patient had been sick, vomited, had backache, and was generally weak all during pregnancy. She had had bronchitis after an attack of measles at the age of eighteen, whooping cough, influenza at the age of thirty-two, tonsillitis, questionable pleurisy, and questionable gonorrhea.

Physical examination revealed a systolic blood pressure of 106 and a diastolic pressure of 96. Examination of the chest revealed dullness and decrease in fremitus, more marked on the left side. The postcervical axillary glands were slightly enlarged. The heart dropped a beat every six to twenty beats. The abdomen was distended with fluid, and there was tenderness and bulging over the flanks and a central tympany in a supine position, with a fluid wave. There were large masses attached to and movable with the uterus. The cervix was soft, dilated, with dullness over the lower lobes, especially the left; menstrual discharge was present. A catheterized specimen of the urine revealed an occasional red blood cell. Hemoglobin was 71 per cent, and leucocytes numbered 8500. X-ray examination of the chest revealed bilateral fluid extending as far as the seventh rib posteriorly.

In view of the latter finding, aspiration of the chest was carried out on August 4 following which the diagnosis of malignancy was questionable. X-ray examination after the aspiration showed some improvement in the chest condition.

On August 16 exploration was performed. A large tumor, the size of a child's head, was found, which had the clinical appearance of malignancy, but which the pathologist reported to be benign. There was marked ascites. The ovarian tumor was very adherent, was impacted in the pelvis, and was difficult to remove. The sigmoid flexure was short. The appendix was abnormal and was not disturbed. No gallstones could be felt. A subtotal abdominal hysterectomy with bilateral oophorectomy and salpingectomy was done.

The final pathologic report showed metritis, chronic salpingitis, and degenerating fibroma of the right ovary.

The patient's convalescence was uneventful and she left the hospital on August 30.

She returned to the Clinic again in August, 1921, at which time she stated that she had been well since her operation; her appetite was good, and she had gained fifty pounds in weight. She was again seen in September, 1921, at which time the general examination was essentially negative and the patient did not wish to have a more complete examination.

CASE 5.—(Mayo Clinic.) A fifty-three-year-old married woman entered the hospital on Nov. 26, 1920, complaining of bloating of the abdomen and some pain between the scapulae. Three years prior to the patient's admission she fell down twenty-two steps, after which the menstrual periods stopped completely and at that time she began to experience pain in the lower abdomen, which was more severe when she attempted to walk. Associated with this pain was considerable bloating, which was very severe at times. Steam-cabinet baths and abdominal massage gave considerable relief. Following an attack of pleurisy in 1915, there had been some substernal pain and moderate discomfort in the interscapular region. There was no evidence of an acid-fast infection, with the exception of occasional night sweats. The gastrointestinal history was essentially negative, and it was noted that there had been some dyspnea on exertion and occasional nocturia. Three years previous to the patient's entry she had been hospitalized elsewhere and had had 40 ounces of

examination showed a growth of fibrous tissue with rather numerous and large cells traversed by vessels having a wall slightly differentiated from the surrounding tissue. A diagnosis of fibroma was made.

Following operation the patient continued to improve, but on December 31 she complained of sharp pain, on inspiration or cough, in the right axilla. She was transferred to the Medical Service for further observation and treatment. Examination of the heart showed apex impulse not seen but felt faintly in fifth space $8\frac{1}{2}$ cm. to the left of the midsternum 2 cm. inside the nipple line. Sounds were regular and of good quality. No murmurs were heard. The pulmonic second sound was greater than the aortic and not accentuated. The pulses were synchronous, equal, regular, and of fair volume and tension. The abdomen was slightly rounded, soft, and tympanitic throughout. There were no masses or tenderness. The liver was at the sixth rib to the costal border; the edge was not felt. The splenic edge was not felt. There was no edema.

On Jan. 5, 1909, friction rub and pain in the side were still present, but aside from this the patient felt better and was up and about the ward all day. Potassium iodide was given, 10 gr. three times a day. She coughed a good deal for twenty-four hours.

On January 9 there was no fluid in the chest. There was a little dullness at the extreme left base behind, but normal breathing was heard at the base. There was a coarse friction all over the left back below scapula and in axilla. The lungs were otherwise normal. She felt very well. There was no pain in her side. The patient was discharged on January 9.

On Nov. 11, 1935, a letter was received from the patient stating that she was in good health and very active. Thirteen and a half years previously (thirteen and a half years postoperatively) she had had to undergo an operation for adhesions of intestines and removal of the appendix and several small tumors. A letter from the surgeon who performed the operation stated that the patient entered the hospital complaining of spotting of blood of two weeks' duration. Preoperative examination showed adhesions about the uterus and a soft, tender mass in the left adnexal region. A preliminary dilatation and curettage was done, with negative findings. On opening the abdomen dense adhesions were encountered; many loops of the ileum were adhered to each other and to a mass in the pelvis. The uterus was completely buried in adhesions. The left ovary was buried in a mass of adhesions and consisted of numerous follicle cysts and fibrous tissue; it was dissected out, and together with the uterus (which was very slightly enlarged) was removed. The appendix was also buried in adhesions; this was dissected out and removed. Kidneys, liver, gallbladder, and upper abdomen were all palpated negatively. The specimens were examined grossly, but no sign of any malignancy was noted, and they were not sent to the laboratory. The patient made an uneventful recovery.

CASE 4.--(Mayo Clinic.) A thirty-six-year-old married woman with one child entered the hospital on July 31, 1917, complaining of a prolapsing uterus and "bleating" of the abdomen. After the birth of her child, three years prior to her admission to the Clinic, the patient had been confined to bed for three weeks, menstruated considerably at the time, and for two or three weeks had felt a dragging sensation continually. After about one year she had noticed the protruding of the uterus, which gradually came down further until it protruded four or five inches. At the same time she had noticed bleating of the abdomen, which was diminished but not entirely reduced after urination, and this complaint had been more marked during the last six months. The patient's appetite was poor. She was constipated at times and passed a yellow, mucous material with the fecal matter. There had been a foul discharge for five months. During the spring previous to her entry she had experienced sweats and chills, with some coughing

and the rest of the abdominal organs were normal, although no specific mention of the liver was made. The mass, which proved to be a benign tumor of the ovary, was removed.

After a stormy postoperative period the patient finally recovered and was discharged on the twentieth day after operation. There had been no return of the fluid except for the withdrawal of 300 c.c. of fluid from the right chest on the fifteenth day after operation. No further chest taps were required.

On check-up two months after discharge, the patient's general condition was excellent, and there was no evidence of fluid in the chest or abdomen.

CASE 7.—(Massachusetts General Hospital.) A fifty-two-year-old single woman entered the hospital on Aug. 4, 1934, with the complaint of changes in bowel habits and dyspnea on exertion of three months' duration. She had begun to have loose watery stools containing mucus, three or four times a day. Shortly after the onset of the bowel discomfort she had noticed dyspnea on exertion. This dyspnea had become more marked and on May 10, 1934, she had been examined and found to have fluid in the right chest. Considerable fluid was withdrawn with marked relief of dyspnea. Subsequent taps at ten- to fourteen-day intervals were necessary to keep her comfortable. About two months prior to admission she had noticed an increase in the size of her abdomen; frequent injections of salyrgan were given with some decrease in the size of the abdomen. There was marked decrease in her general strength and vitality, and it was necessary for her to live an invalid's routine. Her past and family history were negative.

Physical examination revealed that the patient was quite ill with signs of a large pleural effusion on the right and a large amount of fluid in the abdomen. Blood pressure was 120/76. The heart was normal. There was no edema of the extremities. There was no enlargement of any of the peripheral glands. The liver edge was felt, in spite of the large amount of abdominal fluid nearly down to the umbilicus. Pelvic examination revealed a hard orange-sized mass in the left vault.

Routine urine examination was negative other than for the slightest possible trace of albumin and occasional white blood cells in the sediment. Complete blood examination revealed a fairly marked secondary anemia with hemoglobin of 65 per cent. Red blood count 3,100,000, white blood count 12,000. The differential count was normal other than for 73 per cent polynuclears. The red and white cells were normal other than for achromia of the red cells. Repeated sputum examinations were negative. Repeated stool examinations were negative. Nonprotein nitrogen was 39 mg. Serum protein was 7.1 per cent. Blood chlorides were normal. Hinton test was negative. Liver function test was normal. X-ray examination of the chest revealed no abnormalities other than the large amount of fluid in the right chest. Gastrointestinal series and barium enema were negative. X-ray examination of the bones was negative.

Two days after admission 2,300 c.c. of fluid were removed from the right chest with a replacement of 1,500 c.c. of air. The fluid was a typical transudate. Examination failed to reveal the presence of any tumor cells or tuberculous organisms. Guinea pig inoculation was likewise negative. Routine culture of fluid was negative. Abdominal tap revealed an identical fluid.

An exploratory laparotomy and left salpingo-oophorectomy were performed on August 18. The peritoneum was normal. The liver was markedly enlarged. The right lobe came down to the level of the umbilicus, but the liver was perfectly normal in appearance and to palpation. A large amount of yellowish fluid was removed. The spleen was normal. The stomach and intestinal tract were normal, as were the kidneys. There was a small gallstone in the gallbladder, and the pancreas was normal. There was a large solid tumor filling the pelvis. This tumor, which included the left ovary, was removed. The uterus and right ovary were normal.

fluid removed from the chest, and seven weeks later 60 ounces of fluid were removed. The patient had been very dyspneic before her first hospital care and was only relieved by tapping of the chest. Upon entry she still complained of dyspnea and fluid was present in the chest, with moderate abdominal ascites.

The patient's father had died of arteriosclerosis; in other respects the family history was essentially negative. She had been married for twenty-two years but had never been pregnant. Menstrual periods had been normal until three years prior to her admission, at which time they had ceased completely. She had had diphtheria several years previously, influenza in 1898, and pleurisy in 1915.

Physical examination revealed a systolic blood pressure of 108 and a diastolic pressure of 80. An area of dullness to flatness was noted in the lower right chest; no breath sounds were noted; there was an absence of tactile fremitus; whispered pectoriloquy was observed and increased vocal fremitus, amounting to bronchophony. The left border of the heart was found to be just within the anterior axillary line, in all probability displaced and only slightly hypertrophic. The abdomen was dome-shaped, with signs of the presence of considerable fluid.

Urinalysis was essentially negative. Hemoglobin was 73 per cent; red blood cells numbered 4,600,000 and leucocytes 6000. X-ray examination of the chest showed fluid in the right chest to the level of the second rib.

A paracentesis was done on Nov. 30, 1920, and 6½ liters of clear, straw-colored fluid were produced. On Dec. 1, 1920, about 1600 c.c. of clear, straw-colored fluid were aspirated from the right chest and bacteriologic studies revealed no bacteria and no growth of organisms.

Abdominal exploration was carried out on Dec. 9, 1920. A midline incision was made and several liters of straw-colored fluid were evacuated. A large, nodular, and friable tumor (about the size of a large grapefruit) of the right ovary was attached by a rather small pedicle, which was clamped off; the tumor was then removed. The left ovary was about the size of a buckshot and was not disturbed. The uterus was normal in size and position. There was apparently no metastasis to the peritoneum, and the liver contained no metastases.

The pathologic report on the tissue removed showed an edematous degenerating fibromyoma, with the remaining ovarian tissue flattened out over the fibromyoma.

The patient's convalescence was essentially without incident, and she was discharged on Jan. 14, 1921.

Five months later (June 21) the patient returned to the Clinic. She had gained 20 pounds in weight, and her general health was excellent. Abdominal and bimanual pelvic examination failed to reveal any trace of recurrence of the tumor.

CASE 6.—(Leo's case.) A sixty-four-year-old woman was admitted to the hospital on March 25, 1926, complaining of dyspnea, cough, and pain in the right chest of several months' duration.

Physical examination revealed poor general condition and the signs of a large pleural effusion in the right side of the chest, with a mass, the size of an adult's head, in the lower part of the abdomen.

Repeated chest taps were necessary to keep the patient comfortable, 1000 c.c. of fluid being removed every three or four days. The fluid had the characteristics of a transudate and no definite diagnosis could be made by study of it. Tuberculin skin test was positive. Ehrlich's skin test was negative. Shortly after admission nodules developed and became quite severe. The patient ran a slightly elevated temperature.

Because of the doubtful course of the patient and because of the apparent hopelessness of the situation, operation was performed on July 25. The abdomen was opened and a large amount of greenish, yellow fluid escaped and a large mass was found occupying the region of the left ovary. The uterus, the right ovary,

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ABSTRACT OF DISCUSSION

DR. EDGAR A. VANDER VEER, ALBANY, N. Y.—I have reviewed the histories of Dr. Albert Vander Veer and myself for the past forty years but could find no notes on the charts of any condition such as described in this paper. There were a few cases of fibroma of the ovary with ascites but no note was made of any pleuritic effusion. Nowadays we see and operate upon these cases so early that we seldom find ascites and so our attention is more likely to be called to it, and especially if fluid in the chest should accompany it. I do not doubt but that many more of these cases have occurred than Dr. Meigs has reported but that they have gone undiagnosed.

This paper is of as much importance to the internist as it is to the abdominal surgeon for now he can find a cause for some of these cases of so-called idiopathic pleurisy which before had escaped a reasonable explanation.

A point to be learned from Dr. Meigs' paper is the value of an exploratory operation. Some of his cases were thought to be inoperable carcinoma of the pelvis with metastases to the lung, and if they had not had the exploratory operation would have gone on to hopeless invalidism and death. Only in the most hopeless cases should we refuse to make an exploratory incision, for we can never be absolutely certain what pathologic condition we will find within the abdomen.

DR. W. T. DANNREUTHER, NEW YORK, N. Y.—I can add another case to Dr. Meigs' series of seven. The patient was a woman of thirty-six years who was being treated for what her family physician regarded as a normal pregnancy, since he had watched an abdominal tumor develop with a corresponding amenorrhea. Two weeks before I saw her the accumulation of fluid in the right side of the chest was recognized. An internist had been in attendance and had been removing from 300 to 500 c.c. of fluid each day. I made a diagnosis of ovarian malignancy, assuming that the accumulation of fluid in the chest was due to metastasis, although the internist attributed it to a tuberculous pleurisy. A guinea pig had been injected but sufficient time had not elapsed to determine whether or not the pig had developed a tuberculous peritonitis.

The patient was a poor operative risk and about 600 c.c. of fluid had been evacuated from the chest in the morning, a little being left behind. The tumor was however removed without difficulty. There was no fluid in the abdominal cavity. The tissue grossly presented the appearance of an adenocarcinoma, but it was found to be benign. Despite the accumulation of some fluid during the convalescence, it was thought unwise to repeat the paracentesis. The fluid was finally absorbed completely, as demonstrated by the x-ray, and the patient made a complete recovery.

DR. ARTHUR T. JONES, PROVIDENCE, R. I.—In reviewing my records before this meeting I found 6 cases of solid tumor of the ovary that I had operated upon. Only one was a true fibroma, the other five being sarcoma of the ovary. Among 5 cases of sarcoma there were 4 with ascites. In one case of sarcoma and in the single case of fibroma it was not noted whether there was fluid in the abdomen or not. In none of these cases, however, did I note fluid in the chest, but I believe that in the past we may have overlooked it.

The pathologic report showed a very large, solid, firm mass 15 by 7.5 by 7 cm. Its cut surface was of a mottled yellow and white color with streaks of white crossing it in every direction. There were one or two areas which appeared finely granular. A diagnosis of fibroma was made.

The patient made a particularly smooth convalescence and was discharged three weeks after operation. Six months after discharge there was no evidence of chest or abdominal fluid by examination and fluoroscopy. The liver was still enlarged, the lower border being felt about halfway to the umbilicus.

A letter was received from the patient in April, 1935, stating that a fluoroscope showed a normal condition and that her physician had said that the right side and chest looked better than the left, if anything. She was again heard from in December, 1935, and stated that she was feeling perfectly well.

SUMMARY

There have been described in this paper seven cases of ascites and hydrothorax due to the presence of a tumor of the ovary of a nonsecretory type. The importance of such a lesion in medical and surgical problems seems very great, for unexplained pleurisy with effusion and unexplained ascites are problems that occasionally confront our internists. They must be made aware of the possibility of a simple tumor being responsible for such conditions. The surgeon who found ascites and hydrothorax in a patient with a tumor of the abdomen or pelvis might reasonably feel that a malignant lesion was responsible. It is essential therefore that this entity be known to him, for what could be more satisfactory than to cure such a condition by the simple removal of a benign tumor? Many of us have seen ascites suspected as being of malignant origin cured by the removal of a fibroma, when exploration seemed justifiable because the tumor was movable, but who of us would be daring enough to advise removal of a pelvic tumor accompanied by ascites and fluid in the chest? It is evident that such a patient would be doomed as inoperable, unless it were remembered that this particular entity might be due to a fibroma of the ovary. We feel that such a group of cases should make an impression upon many physicians and surgeons. It is hoped that by their making use of the knowledge some women will escape inevitable invalidism.

CONCLUSIONS

1. Seven cases of fibroma of the ovary associated with ascites and hydrothorax are reported.

2. Four cases are from the Surgical and Medical Services of the Massachusetts General Hospital, two are reported in full for the first time from the Mayo Clinic, and one is taken from a paper by Leo in the Italian literature.

3. No adequate explanation is given to explain the phenomenon.

4. The importance of the entity to the medical man and to the surgeon is obvious.

5. The curability of certain seemingly hopeless conditions is emphasized.

THE RESULTS OF INDUCTION OF LABOR IN 750 CASES FROM PRIVATE PRACTICE

A COMPARISON WITH 750 CONTEMPORARY CONSECUTIVE NONINDUCED CASES

ALBERT MATHIEU, M.D., AND ALBERT HOLMAN, M.D., PORTLAND, ORE.

THE purpose of this paper is to estimate the results in 750 cases of induced labor and to compare these results with those of 750 consecutive, contemporary cases in which labor was not induced—all from our combined private practice.

Dale¹ was the first to observe that pituitary extract would cause contraction of the uterine musculature and published his observation in 1906. As this information was buried in a paper on ergot, and as no suggestion for its clinical use was given, little attention was paid to it. Bell,² however, came to the conclusion that pituitary extract would have a clinical use, and after three years of experimentation published his results in 1909. In this publication he gave credit to Hendry for first using pituitary extract to initiate labor pain. Hendry had successfully used an injection of pituitary extract after a Braxton Hicks version to induce uterine contractions in a patient with placenta previa.

Hofbauer³ in 1912 and Watson⁴ in 1913 published reports of successful inductions of labor accomplished by the injection of pituitary extract. In 1915 Bell⁵ set forth a definite routine for the induction of labor by combining the intrauterine insertion of a bougie with 0.5 c.c. doses of pituitary extract twice a day. Bandler⁶ in 1916 used an injection of $\frac{1}{2}$ c.c. of pituitary extract with a bougie or a bag for induction. He also used three injections of $\frac{1}{2}$ c.c. at half-hourly intervals as a diagnostic test between false and real labor pains.

Stein and Dover⁷ in 1917 advocated two small doses of pituitary extract (2 or 3 minims) combined with castor oil and quinine for the induction of labor. They gave the first injection of pituitary extract two hours after the castor oil and the second injection two hours later. They wrote, "If labor pains are elicited, the pituitrin is resumed at intervals of one-half hour; if no pains result, the treatment is stopped and another attempt is made on the third following day, again administering the same small dosage." They reported 34 cases, 17 of which were successful. The mothers did well and the babies were born in excellent condition.

Watson⁸ in 1922 published his routine for the induction of labor. It consisted of castor oil, quinine, and an enema given in the evening, and followed the next morning by 0.5 c.c. injections of pituitary extract until labor pains began. A total of six doses was given if necessary.

Mathieu⁹ in 1927 recommended a modification of the Watson technic, giving quinine and castor oil, and two hours later giving a hot enema followed by pituitary extract in 3 minim doses at half-hourly intervals for as many as fifteen doses if necessary. In order to take advantage of the oxytocic effect of the pelvic engorgement caused by the castor oil, the quinine, and the hot enema, he followed the enema immediately with the first injection of pituitary extract. With 91 patients he had 71 per cent success on the first attempt and 96.7 per cent success with continued attempts at induction. In this same year Hofbauer¹⁰ suggested the application of

One of the cases of sarcoma disturbed me very much, and I thought that with this diagnosis the woman had but a short time to live. An older gynecologist to whom I reported the case said, "She will live a long time. Sarcoma of the ovary cases have a very good prognosis." Much to my surprise, that patient lived and is still, twenty-three years later, in good health. All of the other patients with sarcoma also did very well with the exception of one, a young woman with an enormous sarcoma of both ovaries, who died within a year. Sarcoma of the ovary with fluid appears in the majority of the cases to be very similar to the fibroma which Dr. Meigs has reported with hydrothorax.

DR. T. E. JONES, CLEVELAND, OHIO.—This condition may give rise to unimportant errors in diagnosis, as in a patient of mine, a woman about sixty-five years of age who had been operated upon twenty years previously for cancer of the breast. She was traveling in Europe when the tumor was first noted and was told by a physician in London that there was nothing to be done. She was later examined by at least a half dozen physicians in New York, all of whom came to the conclusion that she had a recurrent carcinoma of the breast. In the next six or eight months there was little change, and I could not understand this if she had carcinoma of the lung. Finally I aspirated the chest and operated on the abdominal tumor. This was a fibroma of the ovary and since then there has been no recurrence of the fluid.

DR. JAMES E. DAVIS, ANN ARBOR, MICH.—I would like to ask whether in Dr. Meigs' cases a blood chemistry study was made and whether Dr. Meigs will express his personal view as to the kind of stimulation or agent that caused the ovary to produce this condition?

DR. WILLIAM T. BLACK, MEMPHIS, TENN.—In the last 7,000 admissions to the Gynecological Service in the University of Tennessee (John Gaston Hospital), there have been 9 fibromas of the ovary. Only one of these cases had fluid in both the abdominal cavity and the chest. In another hospital there were 4 cases of fibromas of the ovaries in the last six years. In only one case was there a large amount of fluid in the abdominal cavity. A small amount of fluid in the chest may be easily overlooked. The fibroma in the case with fluid in the chest and abdomen was found at autopsy in a patient who had not been operated upon. She had in addition arteriosclerosis, chronic cirrhosis of the liver, tubercular adenitis, a dermoid in the other ovary and a fibromyoma in the uterus.

DR. MEIGS (closing).—I think we have overlooked a great many of these cases. Dr. Robert Frank is probably correct in his discussion of Stoeckel's work (Mount Sinai Hospital Journal, 1934). I could not find any but the references I have quoted from the literature of the last twenty-five years. Dr. Lee, in Boston, some years ago in writing of a subdiaphragmatic abscess disclosed the fact that many times there would be fluid in the right side without bacteria.

Replying to Dr. Jones regarding the ovarian sarcomas, in going over the cases at the Massachusetts General Hospital, it was found that those that had a diagnosis of sarcoma made twenty or twenty-five years ago were frequently granulosa cell tumors. The true sarcoma of the ovary had the largest mortality of any of the ovarian tumors that we investigated.

As far as the blood chemistry is concerned, it was noted in the individual case histories that there was nothing extraordinary about it in any case. I cannot answer why the fluid occurs.

castor oil had been given, the patient received a hot enema; and as the enema was being evacuated, 3 minims of pituitary extract were injected. After three or four injections of pituitary extract the membranes were artificially ruptured if they were still intact or if the patient was not definitely in labor. The rupture of the membranes was done under the strictest aseptic precautions, similar to those we used in the actual delivery. The membranes were stripped from the lower segment with the tip of the finger, and if this did not rupture them, they were ruptured by scratching with a blade of an Allis forceps. Some of the amniotic fluid was then allowed to escape. The patient was kept on the operating table for fifteen minutes while we made sure that the presenting part was fitting down against the cervix and while we kept close observation of the fetal heart. The injections of pituitary extract were then continued until the patient was definitely in labor. This method has given us practically 100 per cent success in the last 351 cases.

There were three exceptions in this group. One was a patient who was sent into the hospital for a test of labor to determine whether or not the head would fit into the pelvis. After eight injections, the head fitted well into the pelvis and the injections were stopped. Some days later the patient went into labor spontaneously and delivered normally. The second patient showed a definite idiosyncrasy to the drug and had very severe forceful contractions following the injections. Because of this, all efforts at induction were stopped and the patient went into labor spontaneously some days later. The third patient did not respond to two successive attempts at induction, but went into labor spontaneously two days later. In these three cases the membranes had not been ruptured.

Ninety-eight per cent of our inductions were successful (Table I). A good majority of the failures occurred in the first half of the series. Of late, by the addition of rupture of the membranes, we have been able to increase the incidence of success. Most of the failures were due to lack of cooperation on the part of the patient, a few occurred in nervous women who felt that they could not tolerate the prick of the hypodermic needle, and a few were termed failures because of tonic contractions of the uterus after the first injection. In a few cases, in which the head was floating and could not be fitted in before the attempted induction, and in which the head did fit into the pelvis during the attempted induction, we allowed the patient to go into labor normally. So, where there was a question as to whether the head would fit into the inlet, the attempted induction served as a test of labor.

In a total of 300 cases, in which the membranes ruptured spontaneously before or during the induction or were ruptured artificially during the induction, all were successful on the first attempt after rupture of the membranes except eighteen which required more than one attempt (Table I). There were 170 cases in the group in which

pituitary extract on pledgets of cotton to the mucous membrane of the nose for the induction of labor, with the idea that if uterine contractions became too strong the cotton could be removed. In a series of 26 cases he had seven failures and in another of 54 cases, only 1 failure.

Since the last of the eighteenth century artificial rupture of the membranes for induction of labor has been practiced. In 1928 Jackson¹¹ combined hypodermic injections of pituitary extract with rupture of the membranes in 87 patients. In this series there were no maternal deaths but there were 10 fetal deaths. In 1932 Slemons¹² reported on the use of a combination of castor oil, quinine, rupture of the membranes, and the nasal application of pituitary extract in 132 cases with 100 per cent success and one stillbirth. Guttmacher and Douglas¹³ reported 120 cases with 100 per cent success and 97.5 per cent satisfactory results. Vruwink¹⁴ in 1934 published his results in 172 cases. One hundred and six of Vruwink's patients were treated by rupture of the membranes, with and without intranasal pituitary, with 3 (2.8 per cent) not satisfactory; and 22 patients were treated by simple rupture of the membranes, with 100 per cent success, but several had prolonged latent periods.

In our study of the results of 750 consecutive inductions of labor in private patients, we have combined our cases for statistical study (635 and 115). We feel that this combination of our cases is a proper one, in view of the fact that we practice together in the same office and use almost identical methods. Our indications are practically the same and our methods of induction have been identical, not only in technic, but also in the fact that the inductions have been supervised by the same nurses. And in order that we might add further value to this study, we have compared the results in the induction series with the results in 750 contemporary, consecutive cases (635 and 115) in which labor had not been induced and from which cesarean section had been omitted.

In our first 250 cases, we used a method much the same as that of Watson, consisting of hot enemas, castor oil, quinine, and pituitary extract. We differed, however, from Watson in the use of the pituitary extract so far as we never used any doses larger than 4 minims, and we administered the first injection as the enema was being expelled. After we had used quinine in these 250 cases, we noticed that there had crept into the literature an occasional report of fetal death attributed to the use of quinine in the induction of labor (King,¹⁵ Gellhorn,¹⁶ Torland,¹⁷ McSwinney,¹⁸ and others). Since we had harbored a skepticism that quinine was of particular value in the induction of labor, we discontinued its use and found, as we suspected, that it apparently had nothing to do with the success of induction. We then continued without quinine up to our four hundredth case.

In several of our early cases, when we felt that the induction was particularly urgent, we ruptured the membranes in the process of the induction; but this happened in only 44 of our first 399 cases. Following Slemons' lead, we revised our method so that the induction was carried on as follows: When the induction was started, two hours after

At this point we wish to sound a word of warning regarding the artificial rupture of membranes. This maneuver has some pitfalls. It means the invasion of the vagina and uterus and possible infection. There is always danger of prolapse of the cord. Rupturing the membranes is hazardous to the fetus if the head is not engaged. A high percentage of prolapse of the cord will occur unless the one rupturing the membranes is an experienced obstetrician who can fit the presenting part into the pelvis as the amniotic fluid is lost, and who will observe the fetal heart during the maneuver.

Consider the nervous and anxious patient, whose uterus is tense and irritable, in the last fortnight of her pregnancy. Every evening during this period, when the clothes are removed, contractions of the uterus start, continue in the regular manner for several hours, and cease when the patient falls asleep. We cannot state whether this is a nervous phenomenon or whether it is actually a forerunner of true labor, but we know from clinical experience that patients of this type present the most difficulties. During the induction regular contractions of the uterus start after a few injections of pituitary extract only to stop entirely several hours after the administration has been stopped. As previously stated, this type of patient has given us the most trouble. In our attempts to be absolutely safe, we have preferred to discontinue the attempted induction, to give the patient a sedative so that she would have a good sleep, and to renew the attempt on the following day.

Length of First Stage.—We have estimated in our study only the length of the first stage for the reason that most of our patients were delivered very soon after complete dilatation by means of forceps after episiotomy. For this reason an estimation of the total length of labor would be faulty. In the induced series it was a simple matter to be absolutely exact as to when labor started, since the nurse doing the induction knew almost at once when the contractions became regular. This circumstance, however, did not obtain in the study of the noninduced series because so many times the patient came into the hospital after having been in labor some hours and was unable to determine the exact time when the contractions started. We are quite sure, therefore, that the length of the first stage in the induced series is correct and that in the noninduced series is too low. Table II shows that the first stages of the labors in the induced cases were shorter than in the noninduced cases and that the length of the first stage was shortest in the ruptured membranes group in both series.

TABLE II. HOURS FIRST STAGE

	INDUCED		NONINDUCED	
	ENTIRE SERIES	RUPTURED MEMBRANES	ENTIRE SERIES	RUPTURED MEMBRANES
Primiparas	9.35	9.03	10.66	9.0
Multiparas	3.77	2.68	5.8	2.75

Maternal Morbidity.—In studying the morbidity we used the British standard, classifying all cases as morbid in which the temperature exceeded 100° F. on any two of the bidaily readings from the end of the first to the end of the eighth

the membranes were artificially ruptured. Labor took place on an average of 5.2 hours after the membranes were ruptured. The average length of the first stage was 9.5 hours for primiparas and 3.5 hours for multiparas. There were, however, 11 cases in which it took over twenty-four hours before labor started. If these were excluded from the series, it would be found that in 159 patients labor started 2.4 hours after the membranes were ruptured. This short time before labor started in over 93 per cent of our cases is accounted for by the fact that the uterine contractions had already been stimulated by several injections of 3 minims of pituitary extract given at half-hourly intervals before the membranes were ruptured.

TABLE I. ATTEMPTS AT INDUCTION

	750 CASES		300 CASES AFTER RUPTURE OF MEMBRANES	
Total attempts	988		326	
Success 1st attempt	579		282	
Success 2nd attempt	108		14	
More than 2 attempts	48		4	
Total successes	735	98%	300	100%
Failures	15	2%	0	

In this group of artificially ruptured membranes, there were no maternal deaths and 13 cases (7.5 per cent) were classed as morbid by the British morbidity standard. Of these 13 morbid cases, 7 were due to extragenital causes; viz., 1 to cholecystitis, 1 to mastitis, 3 to pyelitis, and 2 to upper respiratory infection.

In the same group there were 7 dead babies, a fetal mortality of 4 per cent corrected to 1.2 per cent after eliminating 3 cases of macerated fetuses and 2 cases of congenital defects. There were 2 cases of neonatal death (autopsy) which were attributed to atelectasis.

A word of explanation seems necessary regarding those cases in which several trials were made before the induction was successful. We have always been extremely careful in carrying out the routine of our inductions, particularly so in an effort to avoid an injection of pituitary extract after labor had apparently started. In several cases we have purposely stopped the injections when there was any uncertainty as to whether or not the patient was actually in labor—accepting a failure rather than assuming a risk. In most patients we deemed it inadvisable to rupture the membranes until the head was fitting well into the pelvis or well against the cervix. There were a few cases in which several attempts at induction were necessary before the membranes could be ruptured with safety. Once those requirements were met, the membranes were ruptured artificially and the patient went into labor promptly.

mention this fact regarding the cerebral hemorrhages in the newborn for the reason that many of our inductions were done to lessen the hazards of breech delivery and of delivery through a narrow pelvic outlet (Tables IV and V).

TABLE IV. FETAL DEATHS

750 INDUCED			750 NOT INDUCED		
Before induction	14		Before labor	7	
After induction	4		During labor	5	
Neonatal	12		Neonatal	17	
Total	30	4.0%	Total	29	3.88%
Corrected	6	0.8%	Corrected	10	1.3%

TABLE V. NEONATAL DEATHS

	INDUCED	NOT INDUCED
Congenital defects	6	1
Premature, under 1,500 gm.	4	9
Atelectasis	2	4
Cerebral hemorrhage	0	2
Bronchopneumonia	0	1

There were four cesarean sections in the induction group. Two followed unsuccessful trials of labor, one was done for placenta previa, and the fourth was done on an elderly woman who had lost her previous child: after three unsuccessful attempts at induction, a baby weighing 5,413 gm. was delivered by cesarean section. There was no maternal or fetal mortality.

PROCEDURE

Our present method of induction of labor, and the one we consider ideal, has been used in the last 114 cases. At 7 in the morning an enema is given, and at 7:30 pentobarbital is given, the dose depending on the patient's weight. Patients weighing less than 130 pounds receive 7.5 gr., those weighing from 130 to 150 pounds receive 9 gr., and those weighing over 150 pounds receive 12 gr. The patient is asleep within thirty minutes. Then injections of 3 minims of pituitary extract are given and repeated every thirty minutes. After the third or fourth injection, if labor has not started and if the membranes are still intact, they are ruptured artificially unless there is some contraindication. The pentobarbital given before hypodermic injections are started saves the patient any discomfort or apprehension and keeps her tranquil. In this series of 114 cases, in which pentobarbital was used preliminary to the induction, there were no failures and only five which required a second attempt. There were no maternal deaths and the maternal morbidity was 5.3 per cent. The total fetal mortality was 3.5 per cent, and when two macerated fetuses were eliminated the corrected fetal mortality was 1.75 per cent.

CONCLUSIONS

1. After analyzing 750 cases of induced labor from private practice and comparing them with a consecutive, contemporary series of cases

day postpartum. After investigating the many different standards for maternal morbidity, we felt that the British standard was the fairest. It obviated the geographic discord prevalent among the published standards of this country (Table III).

TABLE III. MORBIDITY AND MORTALITY

	750 CASES INDUCED	PER CENT	750 CASES NOT INDUCED	PER CENT
Maternal morbidity (British standard)	53	7.07	50	6.6
Maternal mortality	1	0.13	2	0.27
Fetal mortality (total)	30	4.0	29	3.88
Fetal mortality (corrected)	6	0.8	10	1.3

Toxicity and Idiosyncrasy.—In a total of 6,435 injections of pituitary extract, eight patients exhibited tonic contractions of the uterus severe enough to cause us to discontinue the injections. Four patients developed urticaria after labor. This we attributed to an idiosyncrasy to the drug. There were no maternal or fetal deaths in this group.

There was no incidence of premature separation of the placenta in the induced group, nor was there any case of precipitate labor.

It is our routine to follow our patients postpartum for five months, there being in the average case four or five examinations during that time. While we have no exact statistics on the condition of the cervix postpartum in either group, we are well convinced that induction of labor by the use of pituitary extract and rupture of the membranes does not increase the incidence of cervical injury.

Maternal Mortality.—In the 750 induced cases there was one maternal death. As far as we could determine, the induction had nothing to do with the death.

The patient was a twenty-nine-year-old primipara in whom labor was induced because of a flat pelvis, a large baby, and postmaturity of six days. She received only one injection of 3 minims of pituitary extract three hours before delivery. Labor and delivery were uneventful. Approximately 450 c.c. of blood were lost during the delivery. After the episiotomy had been repaired, after the placenta had been delivered, and after the patient had recovered from the anesthesia, the uterus became boggy and bleeding recurred, with a further loss of about 400 c.c. The uterus was packed and the patient seemed in good condition. Soon she became cyanotic and shocked and died three hours after delivery in spite of supportive treatment, including intravenous injections of glucose and a transfusion of whole blood. There was no indication of premature separation of the placenta. Autopsy was not obtainable. Death was attributed to postpartum hemorrhage and shock.

In the 750 noninduced cases there were two maternal deaths—one due to hemorrhage and shock postpartum, and the other due to a rupture of the uterus and hemorrhage during labor.

Fetal Mortality.—The total fetal mortality in the induced cases was 4 per cent, while that in the noninduced cases was 3.9 per cent. The corrected mortality, eliminating congenital defects incompatible with life and premature infants under 1,500 gm., was 0.8 per cent in the induced cases and 1.3 per cent in the noninduced cases. However, when one considers that in the induced cases there were fourteen in which it was known that the baby had been dead for some time, for which reason the induction was done, one can see that there would be considerable difference in the total fetal mortality rate if labor had not been induced in these patients. In the total group there was only one case of prolapsed cord (that in an induced case) and no death from cerebral hemorrhage or birth injury in the induced cases. We

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ABSTRACT OF DISCUSSION

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—There are three types of induction: the mechanical, the chemical, and the combined methods. If the mechanical method fails to bring about the desired results an element of infection is introduced which makes any number of operative procedures much more dangerous. In the chemical group castor oil is notoriously unreliable, for it practically never brings about induction at full term and in only about 60 per cent after term. Our observation has been that when no uterine reaction resulted from repeated doses of castor oil, mechanical induction was also quite likely to fail. Hence it has become our rule not to attempt mechanical induction in a patient who shows no response to repeated doses of castor oil.

There is another type of chemical induction which I hope will become available in the future, namely the artificial reproduction of the endocrine imbalance which apparently results in the onset of labor. It is not too much to expect that further research will determine quantitatively the endocrine status of the individual patient and thus enable us to determine just which and how much of the various endocrines are necessary to bring about the necessary imbalance.

In regard to pituitrin we must consider the very great differences in individual sensitivity to this substance. Until we are able to determine quantitatively the exact endocrine status of a patient we must run the risk, as we do now, of giving overdoses to oversensitized patients.

Dr. Mathieu's paper brings very forcibly to me the remarkable differences in individual experience which one encounters. Whereas he had no bad results in over 750 cases, I, in less than 50 cases, had four instances of severe tetanic contraction of the uterus which cost the life of the fetus in two cases. In some of these cases the nasal method was used and in others extremely small fractional doses beginning with 0.01 c.c., increased gradually at half-hour intervals. One of the cases of contraction fatal to the baby was in a case started at 0.01 c.c., the tetanic contractions coming on after 0.3 c.c.

The method described by Dr. Mathieu certainly cannot be recommended for the average practitioner. It should be undertaken only by those who know exactly what they are doing, all of the dangers involved, and that the use of this method is only in the line of research.

DR. GEORGE W. KOSMAK, NEW YORK CITY.—The essayist is to be congratulated on the good results obtained from the particular method of inducing labor which he has described. The technic of this procedure impresses me as very satisfactory although one may differ with certain details. However, in discussing this topic, it seems to me—and what I am about to say is not in disparagement of Dr. Mathieu's careful study—that one should deal rather, or perhaps as well, with the broader aspects of labor induction than with a particular method of accomplishing the same. There may be no question about the comparative safety of Dr. Mathieu's procedure, but are we to accept the general philosophy upon which his case series, as well as that of other observers in the field, are based? Dr. Mathieu fails to mention in his paper whether these are routine inductions of patients at term and whether there were other reasons. We should know the premises definitely. It strikes me, however, as a very important point because, if the thought is to go out from this association that labor may become a planned process, the possible sequelae of such propaganda must be given the most careful

in which labor was not induced, we reached the conclusion that the maternal and fetal morbidity and mortality were not increased by induction.

2. Induction of labor was successful in 98 per cent of the cases.

3. Induction was apparently not responsible for the occurrence of any pathologic condition during labor, delivery, or the puerperium.

4. In the last 550 inductions quinine was not used and the results were apparently not affected by its omission.

5. In the last 351 cases, if labor did not start after three or four injections, the membranes were artificially ruptured during induction if there were no contraindications and if they had not already ruptured. We feel that this contributed markedly to the success of induction.

6. In the last 114 cases castor oil was omitted and pentobarbital was given before the hypodermic injections were started. Omission of castor oil in no way affected the success of induction. Pentobarbital has been advantageous in keeping the patient tranquil and free from pain, has not interfered with the success of the induction, and has not affected the vital statistics unfavorably.

7. In the entire 750 induced cases there was no instance of abruptio placentae or of fetal death due to cerebral injury or birth injury. There was one instance of prolapsed cord, in a patient whose membranes ruptured spontaneously.

8. Our study has shown a distinct advantage in favor of the induced series. If one considers that this series seems to include most of those cases which promised trouble (the toxemias, large babies, contracted pelvic outlets, apprehensive and nervous patients, etc.), the maternal morbidity and fetal mortality were surprisingly low: in fact, it appears to us that the induction of labor saved much maternal morbidity and several fetal lives.

9. Furthermore, the combination of induction of labor in our private patients with the ultimate in modern analgesia and anesthesia, and with delivery by forceps after episiotomy, appears to be advantageous as regards maternal and fetal morbidity and mortality.

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incidence of allergy than is commonly supposed. Eight cases were found last year, proved by the sensitization test. We do not use pituitrin in the induction of labor.

We teach that the membranes should not be ruptured prematurely, especially in certain types of cases. Premature babies in the absence of the amniotic sac do not stand the ordeal of labor well. In breech presentations, the undue pressure from the fundus on the after-coming head apparently sometimes causes intracranial injury, and a premature rupture of the membranes in these cases predisposes to prolapse of the cord. If cesarean section is a probability, a premature rupture of membranes increases the danger of postoperative infection, so that this procedure should be reserved for patients who are to be delivered by the vaginal route. An early rupture of the membranes, unless labor occurs within thirty-six to forty-eight hours, may enhance the danger of infection.

It has been shown rather definitely, however, that premature ruptured membranes do not particularly endanger or complicate the case, if the baby is in a good position and is fully matured. Rupture of the membranes in the hands of the average man is difficult in the undilated cervix or where uterine contractions are not occurring. Rupture of the membranes is nevertheless one of the most successful methods of mechanical induction of labor.

DR. ADAM P. LEIGHTON, PORTLAND, ME.—Pituitary extract is a valuable product where indicated, but very dangerous in primiparas if used in the first stage of labor. I have had some experience with it and I believe that Dr. Mathieu's teaching is very dangerous if put into the hands of medical students or practitioners starting obstetrics. To use pituitary extract, routinely in repeated dosage, with rupture of the membranes, is distinctly poor obstetrics. Prolapsed cords, fetal deaths, and uterine rupture must be the answer, occasionally at least.

When I desire to induce labor, the Krause method has always sufficed. It is safe. Introduction of a bougie or two or the use of a small rectal tube bent like a hairpin and pushed up between the uterine wall and the membranes, with tight packing of the cervix with gauze, gives me 100 per cent results.

DR. WILLIAM A. COVENTRY, DULUTH, MINN.—The essayist has spoken about the elimination of quinine. Others speak of cutting out castor oil, pituitrin and the barbiturates. The simple rupture of the membranes will give as good results as any other.

DR. GEORGE M. SHIPTON, PITTSFIELD, MASS.—According to Temesvary's theory the thymus developing into maturity gives the endocrine condition which normally starts labor. He added thymus extract to a small dose of pituitrin and produced a substance called thymophysin that he argued could be given safely. This was severely criticized by the A. M. A., but results are what actually count.

The point has been brought out that it might be convenient where patients come from a great distance to have labor by appointment. I believe that such a condition holds in our community, particularly in winter when the roads are impassable. We have developed a technic which has been applied to a small series of 99 and is much like that brought out by the writer of this paper. It consists in giving the patient nembutal, getting her asleep, and then, after preparation, separating the membranes from the lower uterine segment before rupturing. Immediately upon rupturing the membranes the patient is given 0.5 c.c. of thymophysin. Our routine practice is to keep the hand at the cervix until contractions have started. You cannot, of course, get successful labors if the cervix is not prepared.

As to the length of labor with this procedure I am not prepared to make a definite statement, because during the last two years we have been using paraldehyde analgesia. I believe it does lengthen labor to a certain extent; but why should we worry about a twelve-hour labor that is very comfortable as opposed to a ten-hour labor which might be very uncomfortable?

consideration. I have no doubt whatever that Drs. Mathieu, Watson, and Jackson, as well as Drs. Guttmacher and Douglas and others who have written on the subject, can report excellent results. But does this mean that we are to forget all about the physiologic onset of labor and take this out of Nature's hands by substituting a procedure primarily for the convenience of the doctor and the patient? Are we to set aside all our teaching to medical students about the desirability of preserving intact the bag of waters for the sake of the mother as well as the fetus? Apparently we are asked to forget this. It is true that the increasing incidence of hospital deliveries would make it desirable perhaps to have labor start on the calculated date, and, perhaps, with the increased knowledge of the "safe period," we may gradually come to a point when we actually know the exact date of conception. However, notwithstanding all the propaganda in this direction, it is fair to admit that we cannot be sure of the exact date when pregnancy starts in the majority of cases. Nor do we know that 280 days expresses the full period of ripening. It is possible that some fetuses may be developed fully in less than 280 days and that others may require more time. In view of these uncertainties, is it quite fair to lend support and authority to an idea that labor can be planned for a definite day? I admit the temptation is strong, particularly when patients come from outside of the city or live at some distance from a hospital, to have them go in at a given time for delivery, and women have been led to expect that labor will occur on a given date, when as a matter of fact there is not sufficient evidence on hand to support this. There would remain a considerable proportion of pregnant women in whom the exact completion of parturition would be uncertain.

Personally, I do not believe that it makes very much difference whether a woman goes into labor a week before or a week after the calculated date, if the birth canal is physiologically prepared. I feel, however, that we must accept other criteria for calculating the end of pregnancy than the lapse of a prescribed number of days. The cervix offers perhaps the best guide, and Dr. Mathieu fails to state in his paper whether the condition of the cervix was taken into consideration in his induction procedure.

Done under hospital auspices by experts, there is no question but what the method which Dr. Mathieu describes may be very effective. It may be for the best interests of his patient or those of any other expert obstetrician. But the fact cannot be set aside that the majority of confinements are attended by general practitioners, who fortunately still rely, and should continue to rely, on Nature's own devices for terminating pregnancy by bringing on labor at the proper time. We are not as yet fully informed about the causes for the onset of labor. Whether it is an endocrine impulse or something else remains to be seen, but there must be some inherent motive in the pregnant woman or a combination of motives which brings about the onset of pain after the passages are prepared for the birth of the child. Are we going to substitute a therapeutic procedure for a physiologic process? I wonder whether the time is ripe for this.

The literature of recent years, as Dr. Mathieu has pointed out, shows the records of an increasing number of observers who have successfully terminated pregnancy by one means or another, either in the presence of definite indications or simply at the calculated term. This, however, as I have ventured to imply, is not the sole question. The question at issue still remains: have we the right to assume that Nature's plans for terminating pregnancy should be set aside and our own mechanical or other devices substituted?

DR. WILLIAM T. McCONNELL, LOUISVILLE, KY.—In our clinic we reserve induction for some definite condition. We have found that quinine is not only ineffectual but the high incidence of allergy renders it a drug that should be used with caution. Castor oil, on the other hand, is a drug which shows practically no allergic symptoms. We have found that pituitary extract gives a much higher

We are now teaching a great deal of prenatal care in obstetrics. But, are we sure that a great deal of prenatal care is not merely a matter of going through the motions? Insufficient attention is being paid to the estimation of the pelvic outlet, and too often a baby is allowed to develop to a point where it is too large to come through the outlet, or a breech presentation is allowed to continue to term or past term when induction ten or twelve days before term would insure a much lower mortality for the baby.

New procedures and improvements over old methods are slow to gain prestige in the medical field. And, in closing, may we remind you that in the early part of the nineteenth century, when supravaginal hysterectomy was first being advised, a certain group of sedate old London surgeons refused to consider the operation because, as they said, when the uterus was amputated at the internal os, an opening would be left through which the wind might whistle.

PLACENTAL VARIATION

AN ANALYTICAL DETERMINATION OF ITS CLINICAL IMPORTANCE

L. A. CALKINS, M.D., PH.D., KANSAS CITY, KAN.

(From the University of Kansas Medical School)

W. P. MANTON published a paper in 1907 on "The Relationship of the Weight of the Placenta to the Weight of the Newborn Child." This was the first attempt in this country to study the significance of placental size. Previous to this, in England and on the Continent, contributions along the same line had been made by Bustamente (1868), Kruger (1877), Mackness (1889), Blancke (1895), and Sfameni (1901). No contribution of note followed Manton's paper until that of LaVake (1924) which was a study of the relationship of surface area of the placenta to the birth weight of the child. Adair (and Thelander) in 1925 studied the relationship of placental weight, area, volume, thickness, and specific gravity, all in their relation to the weight of the baby. This was the first extensive piece of work on placental morphology and was closely followed in 1926 by the elaborate paper of Westermarck, which was a study of the relationship between placental weight and fetal weight in 19,000 cases. This very large number of cases enabled Westermarck to derive very smooth curves of relationship, which curves he believed to be logarithmic in nature and he computed formulas in which the weight of boy babies and the weight of girl babies was each represented as a function of the logarithm of the weight of the placenta. A similar piece of work was reported in 1930 by Aberle and Morse, wherein a series of 4,000 cases was studied for the closeness of relationship between the weight of the placenta and the weight of the infant. They found a very high degree

DR. IRVING W. POTTER, BUFFALO, N.Y.—I have never induced labor and no man working with me has done so under my supervision. We believe in terminating pregnancy when it is necessary, but we believe in letting the first stage of labor alone. That is not the stage that does any harm or causes the patient any suffering. We do not use phenobarbital and never give pituitrin when the baby is in the uterus.

There is no condition in our experience that produces the shock that is produced by the interference with the first stage of labor. In our work of version and extraction we have always advocated that the patient should go through the first stage of labor, that the lower uterine segment should be obliterated and the os easily dilated.

I want to call your attention also to the ill effects of pituitrin used in cesarean section. When we used to put it into the body of the uterus, the patient would leave the operating room in splendid condition, but in an hour or an hour and a half something would sometimes relax and she would have an uncontrollable hemorrhage. We have now stopped the use of pituitrin in cesarean section and have no more secondary or postpartum hemorrhages.

DR. F. S. KELLOGG, BOSTON, MASS.—The point of main interest to me is whether or not induction by any of these methods works well in the primipara, particularly in preeclampsia, where induction is so often necessary. I have tried to make a study of this phase of the subject and it is impossible from the literature. Most of the time induction works very well, but occasionally it fails, and we are forced to get out of a difficult situation by some not ideal means. I would urge in this connection that when authors report a series of cases of induction, they segregate the preeclampsia cases from the others, indicating parity and condition of cervix, and report them separately.

DR. R. T. LAVAKE, MINNEAPOLIS, MINN.—I wish a paper such as this could specifically state that its aim is to demonstrate the relative security a man may feel when he is called upon to use this method for a definite indication. In going through world literature and trying to find a reason why maternal mortality and morbidity are greater in this country than in many others, it has impressed me that the answer is that we hold a less philosophic view of obstetrics and interfere too frequently. I believe we should interfere only upon pressing indications and never unless we would demand such interference in our own immediate family.

In my part of the country many general practitioners read these papers and when they read a paper like this they do not always realize that such success is largely dependent upon perfection of surroundings and perfection of judgment and technic. If this is not emphasized, I am certain that many men will court disaster and increase their maternal mortality and morbidity.

DR. MATHIEU (closing).—It has been the intention only to present results in 750 cases of induced labor compared with 750 consecutive, noninduced cases. Due to the time allotted it was not possible even to mention the matter of indications. There is no thought whatever of regarding this procedure as routine and induction is done only when indicated.

When Dr. Kosmak raises the question of whether or not facts in this paper should be taught, we think he is leaning backward. Since there are no scruples concerning the teaching of cesarean section, vaginal hysterectomy and other major operations to medical students, there should be no scruples in teaching them the best and safest methods of induction of labor when indicated.

The presentation of our results shows that this method of induction is infinitely better than the old-time bag or bougie method, in view of the fact that there was only one case of prolapsed cord in the entire series and no case of abruptio placentae. When induction is indicated, we think it should be done more or less in this manner.

A similar curve representing the relationship between age and placental area is shown in Fig. 2, and the coefficient of correlation here is $+0.112 \pm 0.016$. This coefficient is sufficiently large to indicate that

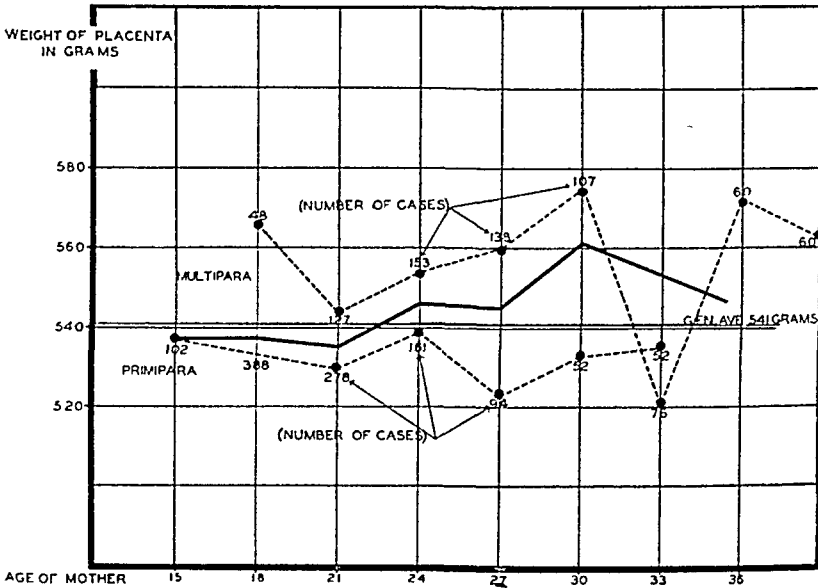


Fig. 1.—Weight of placenta plotted against age of mother. The apparent tendency for the placenta to increase in weight as the mother becomes older is not real. It is due to the greater proportion of multiparas (upper broken curve) and lesser proportion of primiparas (lower broken curve). The separate curves of multiparas and primiparas show no tendency to either rise or fall with increasing age of mother.

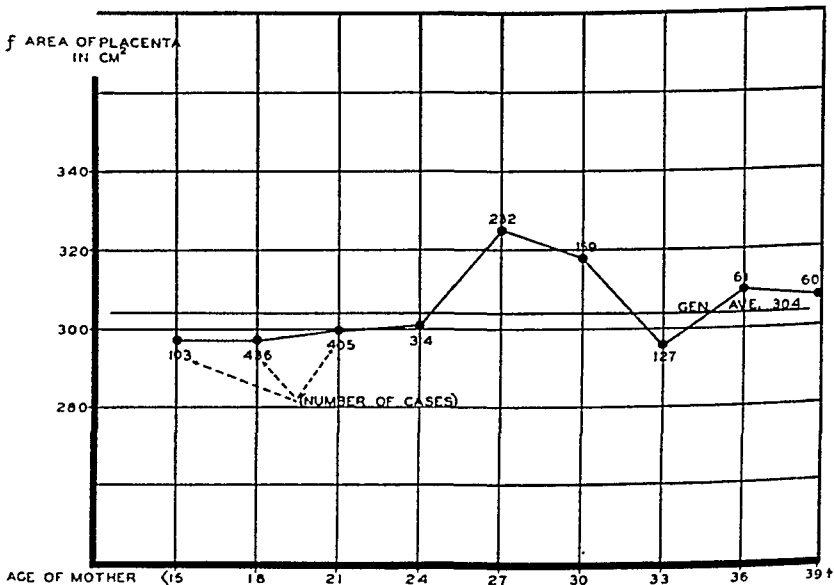


Fig 2.—Area of placenta plotted against age of mother. Very apparent is the conclusion that age of patient has no effect on the area of the placenta.

there is a definite correlation, mathematically speaking, between placental area and age of the mother. It is, however, so small as to be of no clinical importance, and it is probably fair to assume, from a practical point of view, that there is no definite correlation

of correlation as represented by a coefficient in excess of plus 0.5. The relationship for boy babies was slightly closer than that for girl babies but within the same numerical category.

It would seem then that interest in placental size has very largely centered on the relationship between placental magnitude and the weight of the baby. Pastore within the last year casually remarked that "blood loss in relationship to the weight and mean diameter of the placenta showed no definite correlation." Similar casual references may also be found in articles on related subjects but an ordinarily careful search of the literature fails to reveal any concerted effort to find possible causes of placental variation or other possible effects than that noted in the now well-established close relationship between placental size and infant weight.

This present study represents an analysis of some 2,000 consecutive deliveries with the intention of determining whether placental weight and placental area are correlated with any or all of: maternal age and parity, maternal height and weight, duration of pregnancy, fetal weight and height, and blood loss in the third stage of labor. Regression line curves have been plotted to present a visual picture, and coefficients of correlation have been computed as a more exact representation, and, therefore, more conclusive estimate of any possible relationship. The placental weight was of the organ with membranes and cord attached, and the placental area was studied by multiplying the width of the placenta by its length, thus obtaining an area in square centimeters considerably larger (nearly one-third) than the actual area of the placenta. It has been mathematically demonstrated that the error inherent in determining "relative" areas of this type in a large series of cases is sufficiently uniform that the values, thus obtained, are quite as reliable as the "true" areas would be.

AGE OF THE MOTHER

The weight of the placenta as abscissa was plotted against the age of the mother as ordinate and the solid line of Fig. 1 resulted. At first glance there seems to be a tendency for the weight of the placenta to increase as one passes from the younger to the older age groups. That this tendency is apparent rather than real is made obvious when one separates the patients into the primipara and multipara groups. Curves are plotted for each of these two groups, and there is no such tendency to "rise" in either of these latter two (broken line) curves. The coefficient for the primiparas was $+0.058 \pm 0.014$, and for the multiparas $+0.092 \pm 0.024$. In neither instance is the coefficient definitely more than four times its probable error, and it is, therefore, not significant.

as to suggest the very definite possibility that the apparent large size of the placentas in third and four pregnancies in this series is a chance finding and not to be relied upon.

HEIGHT OF THE MOTHER

A study of Figs. 3 and 4 shows quite conclusively that there is no definite relationship between maternal height and placental size, as

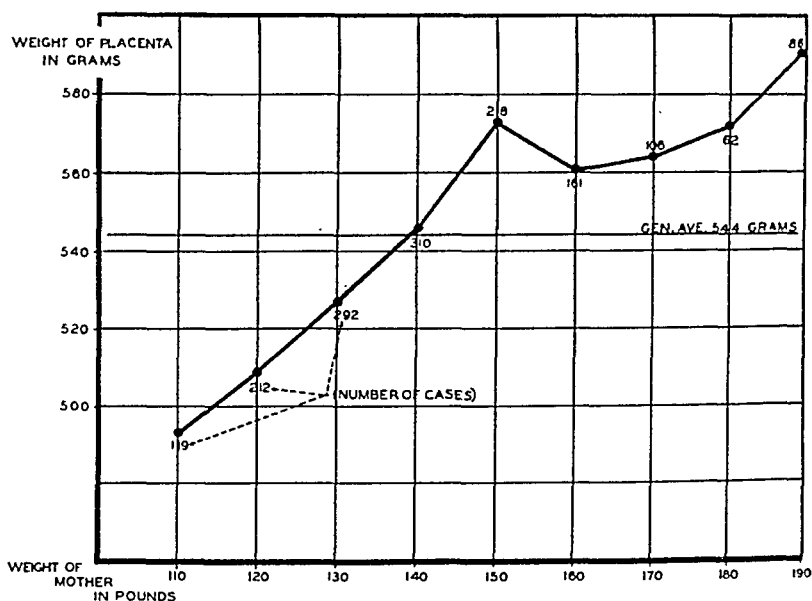


Fig. 5.—Weight of placenta plotted against weight of mother. Clearly the heavier mothers have the slightly heavier placentas.

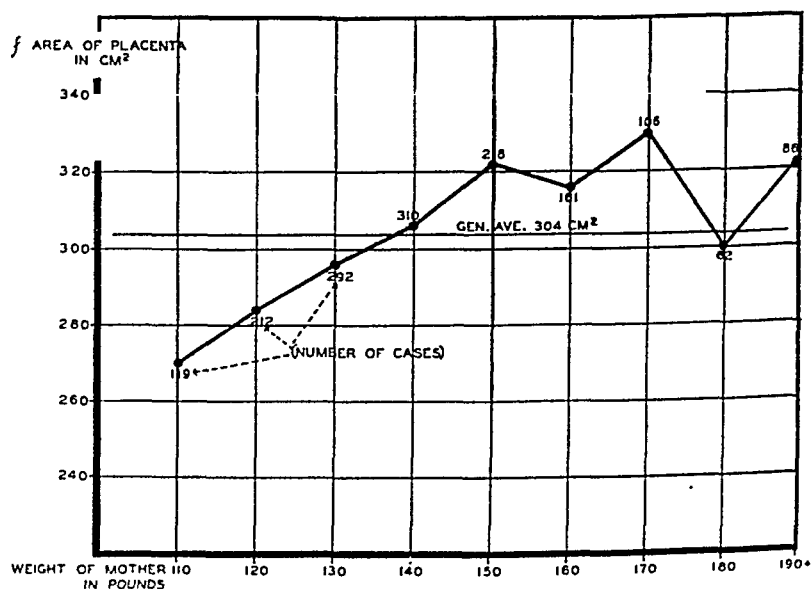


Fig. 6.—Area of placenta plotted against weight of mother. Clearly the heavier mothers have slightly larger placentas as shown by this and the preceding graph.

there is in the curves no definite tendency for placental weight and area to increase as one passes from the shorter to the taller groups, and the coefficients (for placental weight $+0.09 \pm 0.016$, and for placental area $+0.054 \pm 0.016$) are too small to be significant.

PARITY OF THE MOTHER

A study of the effect of parity on placental weight and area resulted in very peculiar curves. The third and fourth pregnancies seemed to produce larger placentas than the earlier or later pregnancies. The

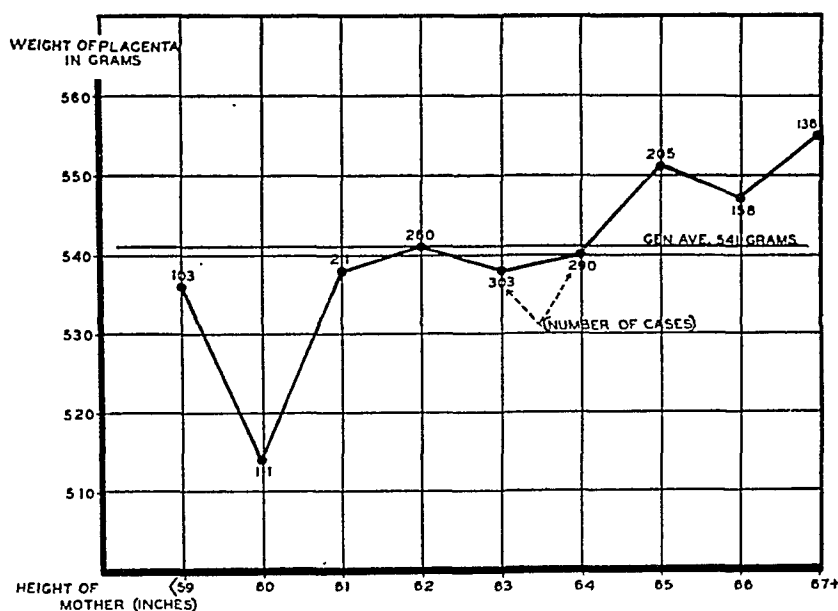


Fig. 3.—Weight of placenta plotted against height of mother. This curve and the one in the following chart indicate that height of mother has no appreciable effect on placental size.

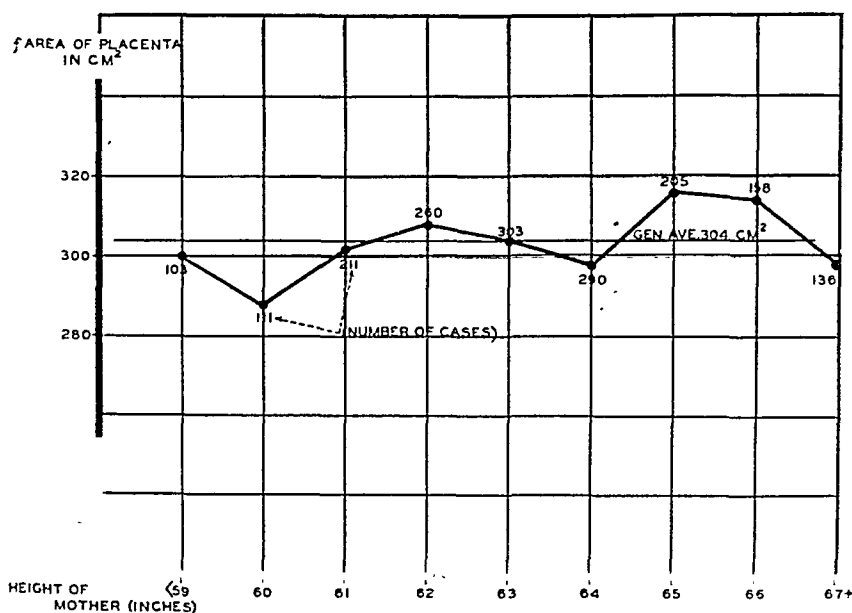


Fig. 4.—f Area of placenta plotted against height of mother. This curve and the one in the preceding chart indicate that height of mother has no appreciable effect on placental size.

number of cases inspected (160 third pregnancies, 84 fourth pregnancies) is too small to make this finding entirely reliable and a larger series must be studied before a final conclusion can be drawn. The coefficient of correlation for placental area was $+0.084 \pm 0.016$, so small

that there is some sort of definite relationship between maternal weight and placental size. Whether this is a relationship between basic (non-pregnant) weight or a relationship between weight increment during

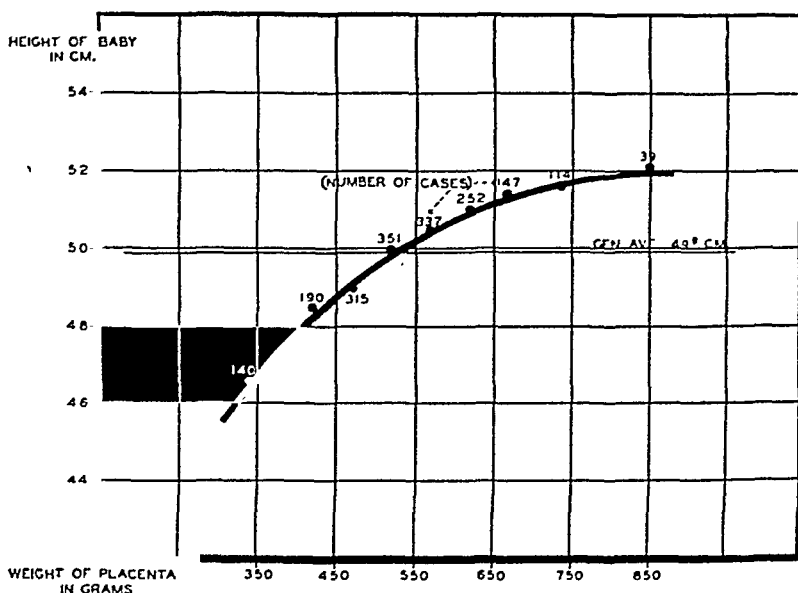


Fig. 9.—Height of baby plotted against weight of placenta. The larger placentas are found with the larger babies. We here show the effect of the placental weight on the baby's height.

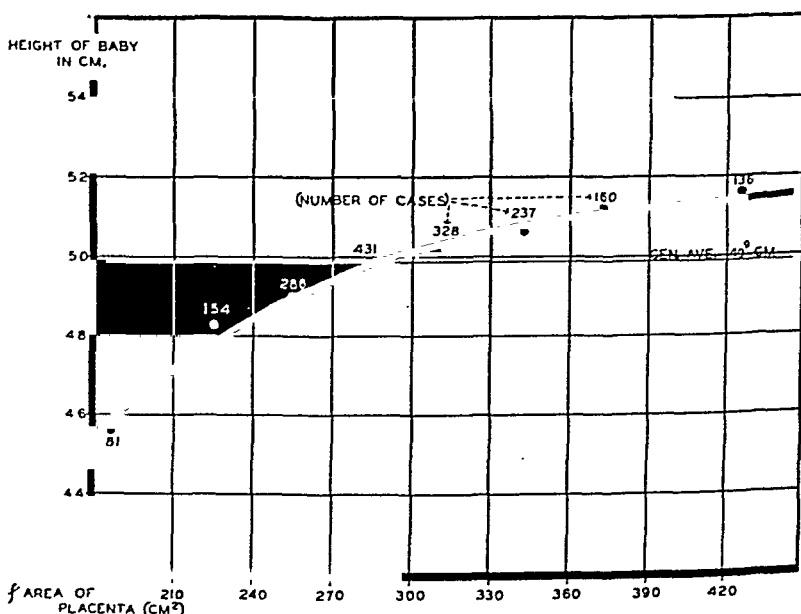


Fig. 10.—Height of baby plotted against f area of placenta. Placental area is a factor in determining height of baby.

pregnancy and placental size, we are not able to say, as our records did not allow a complete study of weight gain in pregnancy.

DURATION OF PREGNANCY

Here we find a very high degree of correlation and a definite tendency for the curves to rise as we pass from the pregnancies of shorter

WEIGHT OF THE MOTHER

Maternal weight taken just prior to delivery and studied in a similar manner (Figs. 5 and 6) showed a somewhat different result. There

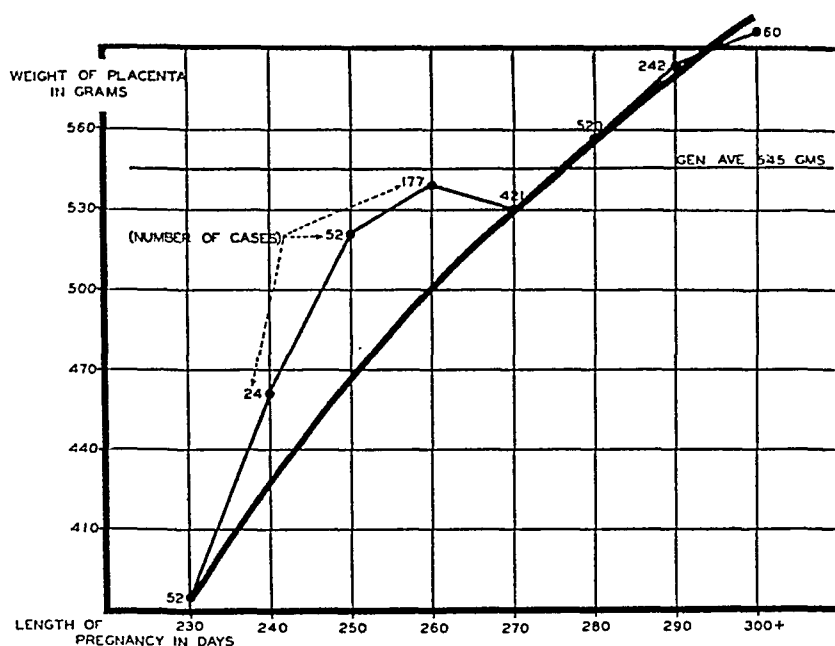


Fig. 7.—Weight of placenta plotted against duration of pregnancy. This curve shows clearly that the size of the placenta increases as pregnancy advances: the increase closely paralleling the growth of the baby.

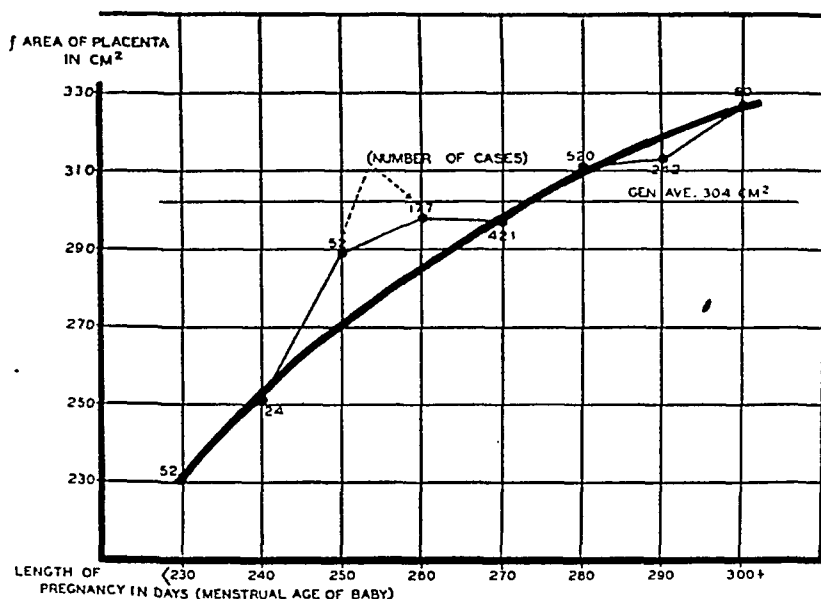


Fig. 8.—Area of placenta plotted against duration of pregnancy. This curve is closely comparable to that obtained when baby's height or weight is plotted against its menstrual age: continuing growth with negative acceleration.

seems to be in the curves a definite tendency for the placental size to increase as one passes from the lighter to the heavier groups of patients and the coefficient of correlation for placental weight was $+0.260 \pm 0.016$; that for placental area was $+0.142 \pm 0.017$. This would indicate

HEIGHT OF THE BABY

One might expect to find here a similar relationship to that previously noted by several authors in connection with their study of infant weight, and such are the results obtained (Figs. 9 and 10). The smaller placentas are very definitely associated with the smaller babies

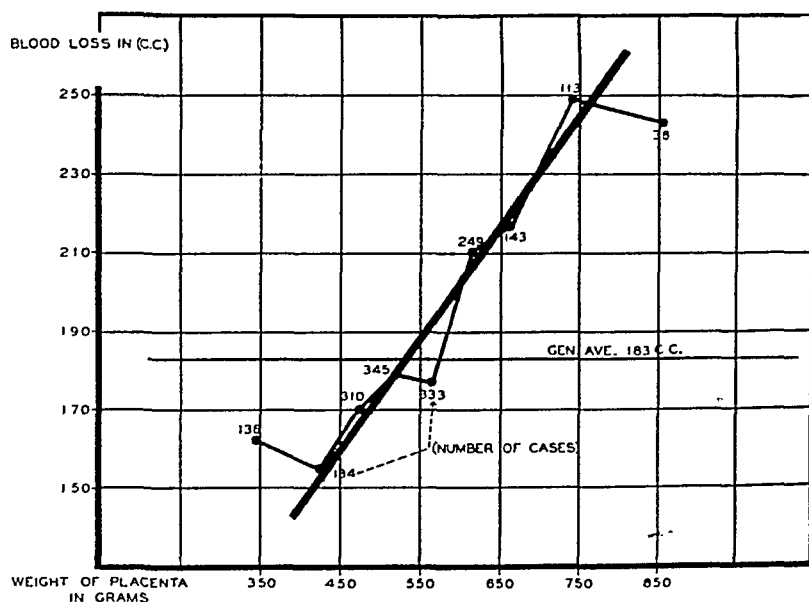


Fig. 13.—Blood loss plotted against weight of placenta. The heavier placentas are associated with greater blood loss.

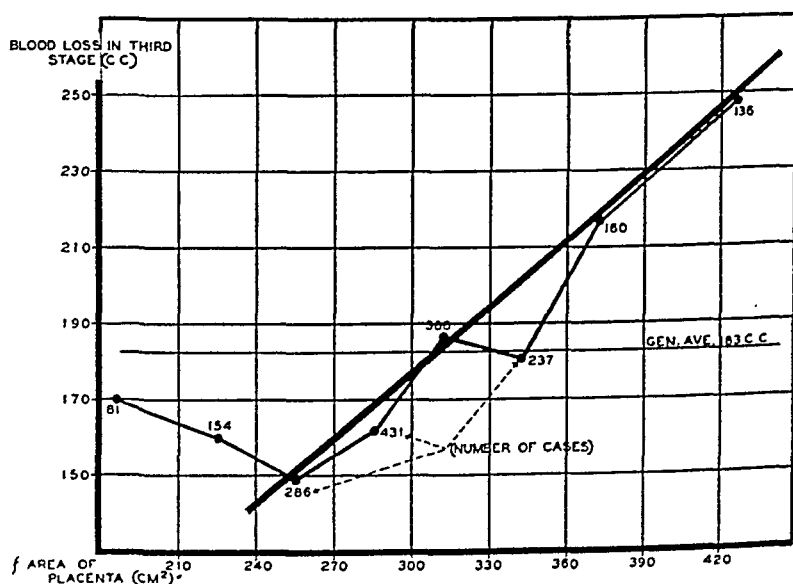


Fig. 14.—Blood loss in third stage plotted against f area of placenta. This graph shows third stage blood loss to be directly proportional to the size of the placenta. (Placental size is only one of many factors affecting this blood loss.)

and the larger ones with the larger babies. The coefficient for placental weight was $+0.45 \pm 0.01$, and for placental area $+0.371 \pm 0.014$. These are very high correlations and approach in magnitude those previously obtained by other authors for the relationship between placental size and weight of the baby.

duration to those of longer duration (Figs. 7 and 8). These findings are exactly in accord with what we might expect, but inasmuch as there are many statements in the literature to the effect that placental size is determined very early, these results are of definite interest. The

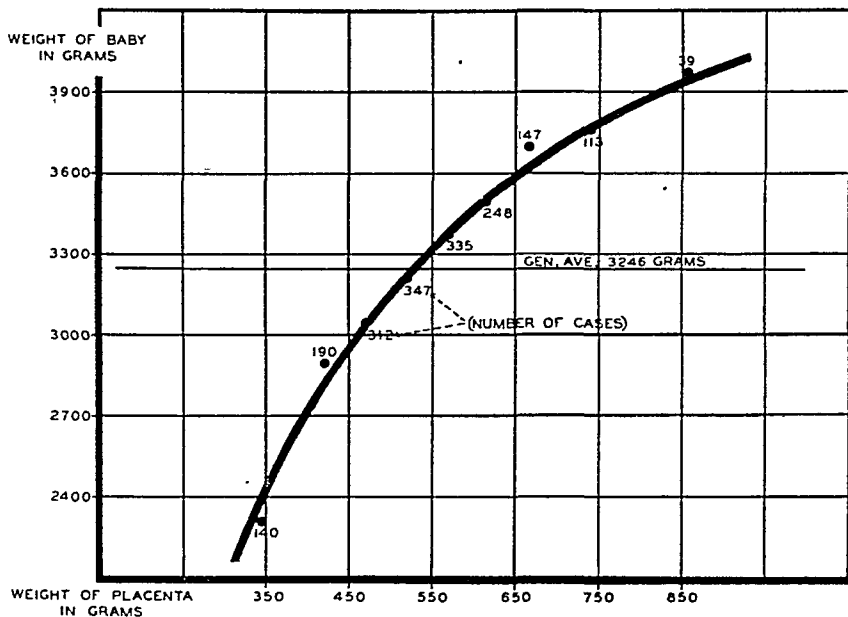


Fig. 11.—Weight of baby plotted against weight of placenta. The heavier placentas produce the heavier babies. The relationship is not exactly a direct proportion.

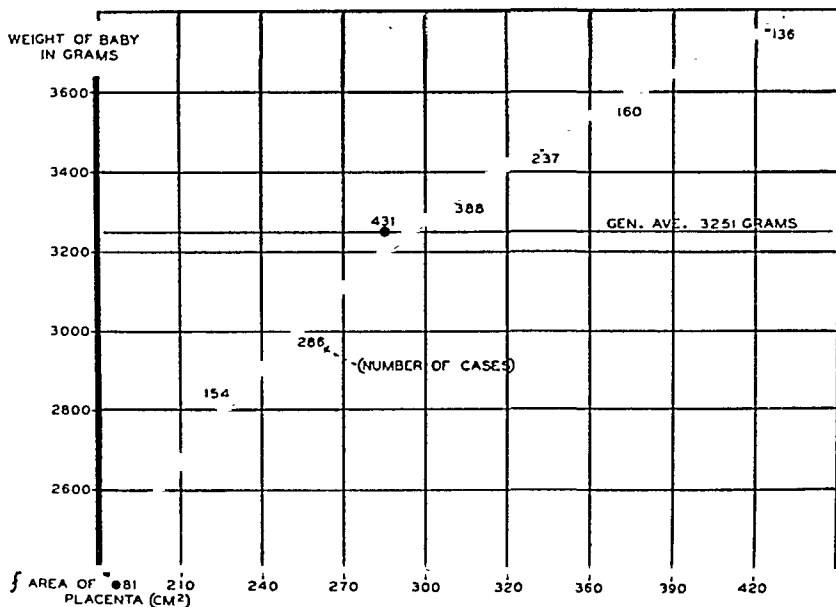


Fig. 12.—Weight of baby plotted against f area of placenta. Placental area very largely influences the weight of the baby.

coefficients were: for placental weight $+0.33 \pm 0.01$, and for placental area $+0.239 \pm 0.016$. This is a rather high degree of correlation, particularly that between placental weight and duration of pregnancy (it is in the same numerical category as the relationship between height and weight of adult men).

Comparison of the data on placental weight with those on placental area would indicate that the latter is less important than the former, because the coefficients of correlation in every instance (where a definite coefficient was present) were less than the coefficients for placental weight. It would seem then that the determination of placental weight alone would be quite sufficient for clinical purposes and that the addition of placental dimensions adds little, if anything, to the value of our clinical charts.

CONCLUSION

A study of some 2,000 consecutive deliveries for the significance of placental weight and (a function of the) placental area in their relationship to maternal height, weight and age; the duration of pregnancy; the parity; fetal height and weight; and blood loss in the third stage of labor indicates that there is no relationship between these measures of placental size and those of the other factors, except fetal height and weight and duration of pregnancy. Possible relationships between placental size and blood loss in the third stage of labor, and between placental size and maternal weight are so small as to not possess any considerable clinical significance.

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ABSTRACT OF DISCUSSION

DR. BENJAMIN H. CARROLL, TOLEDO, OHIO.—Dr. Calkins has carefully studied 2,000 cases and has charted a placental relationship to the baby and to the mother. Practically all investigators agree as to this relationship and, considering their common origin, this relationship would be naturally expected.

Hereditary characteristics and environment play an important rôle in the development of the baby, and I see no reason why they should not affect the physical characteristics of the placenta as well. It would be interesting to know some of the physical characteristics of the father in this group and also of those mothers where the blood chemistry was not normal or where there was some endocrine disturbance.

DR. LAWRENCE M. RANDALL, ROCHESTER, MINN.—Dr. Calkins has mentioned the gain in weight of the mother during pregnancy. We are now making an attempt to correlate the mother's and the baby's weights, comparing the mother's gain with the area of the placenta. We did not weigh the placentas and our data are still too incomplete to give final conclusions.

DR. JAMES K. QUIGLEY, ROCHESTER, N. Y.—Does this series of cases take note at all of postmaturity? In 2 cases of unexplained stillbirths of large babies, postmature, the rather ingenious theory was propounded that the placenta was

WEIGHT OF THE BABY

Our results in the study of infant weight correspond very closely to those of Adair, Westermarck, and Aberle and Morse. The curves (Figs. 11 and 12) "seem" to be logarithmic in type, and the coefficients are $+0.56 \pm 0.01$, and $+0.422 \pm 0.013$. Our results are, therefore, in close agreement with previous investigators.

BLOOD LOSS IN THE THIRD STAGE

The blood loss associated with the third stage of labor was measured after the technic described in previous publications and the study of the relationship of this blood loss to placental size is shown in Figs. 13 and 14. The coefficients were found to be $+0.15 \pm 0.015$, and $+0.145 \pm 0.016$. This would indicate that there is a definite, though small, relationship between the size of the placenta and blood loss during the third stage of labor. This finding is in quite close agreement with the relationship previously noted in another publication between the size of the baby and the blood loss in the third stage of labor. The relationship is probably so small as not to be of particular value in the care of the individual patient and remains, therefore, largely a point of academic interest.

SUMMARY

There is apparently a very close relationship between both height and weight of the baby and placental size. The next closest relationship exists between duration of pregnancy and placental size. This relationship, however, is less than that between the size of the baby and the size of the placenta, and in this same series of cases there is a much closer relationship between duration of pregnancy and size of the baby ($+0.430 \pm 0.021$) than there is between duration of pregnancy and size of the placenta. The evident conclusion is that whereas the placenta continues to grow in the latter part of pregnancy, it does so at a relatively much less rapid rate than the baby.

The apparent (low degree of) correlation between blood loss in the third stage of labor and placental size is again perhaps more apparent than real, as the correlation between blood loss and infant size in this series shows a coefficient ($+0.216 \pm 0.016$) somewhat larger than that between size of placenta and blood loss. It would seem then that the larger placentas are associated with greater blood loss only because they are also associated with larger babies. Perhaps the greater distention of the uterus associated with the larger babies is a more important factor in the production of blood loss than the larger placental area of attachment. Indeed, one might doubt whether a large placental site produces any greater blood loss than a small placental site. Physiologically there should be no difference.

with the stem pessary over a long period have been very satisfactory, and it has seemed to me worth while to discuss this subject, which may seem to many of you more suitable on a program of the early nineties than of today.

Modern authorities express varying opinions about them, as a rule favorable, provided they be used with discretion.

Child, in a contribution on sterility and conception (*Gynecological and Obstetrical Monographs*), condemns them in no uncertain terms and quotes Emmet of an earlier era to the same effect.

Novak, writing on menstruation and its disorders in the same *Monographs*, is rather guarded in recommending them to relieve dysmenorrhea and says the principal objection urged against them is that they may cause a troublesome endocervicitis. He quotes Carstens and Beyea as advocating them.

Graves, in his textbook, says, "The use of intrauterine pessaries is unsurgical in principle and may be followed by inflammatory processes in the tubes, of which we have observed two instances. Nevertheless, even with this risk, the procedure is considered justifiable and is very widely employed. It should be left in from six weeks to two or three months."

Crossen advises the use of a stem in suitable cases. "After dilating and curetting, it is well to introduce a stem to maintain the opening over a period of one to several weeks."

Bland, in his textbook, describes their use but warns that they cannot be employed with impunity or carelessness and that they are not without danger. They are allowed to remain in for three or four months.

Curtis says that for dysmenorrhea a most satisfactory procedure is thorough dilatation with insertion of a metal stem to be left in for six weeks. Complete cure results in more than 50 per cent of the cases and the majority experience considerable relief.

C. Jeff Miller, in Curtis' *Obstetrics and Gynecology*, says, "If a stem of the Baldwin type is used in connection with the operation of dilating and curetting, the percentage of good results is considerably improved. I have had personally from 50 to 60 per cent of permanent cures by this method, 40 per cent by plain curetting, and I have never seen infection follow its use in the properly selected cases.

The purpose of the stem is to overcome a possible obstruction, first, by mechanically straightening out any flexion, and second, by maintaining the internal os and cervical canal somewhat dilated and patulous so long as the stem is worn, and to some extent this will usually be permanent.

Its most important function is to stimulate the normal slow rhythmic contractions of the uterus, which induces a much better blood supply, the most rational treatment possible for a small poorly developed muscular organ. That the uterus is constantly working to expel the stem is shown by the way a suture, used to hold certain varieties of pessaries in place, will gradually cut through a wide area of dense cervical tissue. The improved blood supply is evident from the increased menses which, in a few cases, may become too excessive.

insufficient for the size of the baby. I believe Dr. Calkins did call attention to the fact that the size of the placenta is not in proportion to the increase in the weight of the baby.

DR. R. T. LA VAKE, MINNEAPOLIS, MINN.—My own work in this field has aimed merely to find out whether the weight of the child was influenced by the size of the placenta or by the diet of the mother. I found that there was no correlation between the diet of the mother and the size of the child. Apparently the size of the child was correlated with the area of the placenta, but you could feed the mother almost on lettuce alone, and her baby and the placenta would be large or small, depending probably upon hereditary influences. In cases where much placental infarction was present, the babies were relatively smaller than in cases with equal-sized uninfarcted placentas.

DR. CALKINS (Closing).—I am not prepared to discuss placental insufficiency either on the basis of size or of destroyed placental tissue by the formation of infarcts. We did have in this series one patient who went somewhat overtime according to her history, whose placenta was very small and whose baby was also very small. We felt that this perhaps was a case of placental insufficiency, but so far as I am able to find in the literature there is no authentic entity of placental insufficiency on the basis of size. Adair, in his paper, noted that of a large number of stillbirths—small babies at or near maturity—the majority had placentas considerably under the average size.

RESULTS WITH THE INTRAUTERINE STEM PESSARY

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THE presentation of this paper has been prompted by an apparently widespread opinion that a stem pessary is a very dangerous contrivance and exceedingly likely to produce pelvic infection.

On one occasion a patient, on whom I had used a stem with only good results, was informed by another physician that I should not have used such a dangerous device and that my treatment approached malpractice. It usually develops that such critics have had no personal experience with these pessaries, but are simply echoing a tradition handed down from a time when their limitations were not clearly defined and when bad results occurred from their injudicious use.

In examining candidates for the National Board of Medical Registration on the subject of gynecology, I have had the curiosity to ask many of them what they knew about stem pessaries. The majority knew nothing at all. The others said either that they were a quack contraceptive device, or that they were used for dysmenorrhea but were very dangerous. The replies of these graduates of a number of medical colleges may give some indication of the views of their different instructors.

In our eagerness to try new methods we are prone to forget older well-tried ones that are still too valuable to be discarded. My results

some cases a cervicitis may be the cause, and it is surprising how often a marked cervical erosion will be found in antelexions in virgins in their teens. The question then arises, may this be due to faulty drainage due to the antelexion. I think it may be at times and do not therefore consider an erosion of the cervix as a contraindication to the use of a stem. Many times I have seen it clear up with the stem *in situ*. If it persists it may be treated on the subsequent office visits with silver nitrate or light cauterization without disturbing the stem.

The rigidity in many cases, even in young individuals, is undoubtedly due to endometriosis. It may be impossible to prove this without an abdominal operation but I am convinced the condition is far more common than is generally suspected or than the pathologic reports on tissues removed at operation would indicate.

This discussion of pelvic rigidity and endometriosis leads up to the question whether a stem should ever be used when there is evidence of any pelvic inflammatory process. The presence of such a condition or even the history of a previous attack of inflammation is always given as a positive contraindication for the use of a stem. Endometriosis may produce an inflammatory reaction with thickening and adhesions, but this need not be an infective process but more a chemical irritation from repeated small areas of hemorrhage. True, a bacterial infection may be superimposed, as is sometimes found in infected chocolate cysts, but this is exceptional. A suspected endometriosis, even with apparent adhesions of the lateral structures, has therefore not prevented my using a stem in many such cases, provided I felt reasonably certain the inflammatory process was neither puerperal nor gonorrheal in origin.

The stem pessary is a valuable aid in another class of cases in which there may or may not be dysmenorrhea or irregular periods, viz., retrodisplacements that one attempts to cure by the use of a retroversion pessary. A flabby atonic uterus may double back upon itself even if the cervix be held well back in the posterior fornix with a Smith pessary. A stem within the uterus will generally prevent this and improve the tone of the muscle. In nervous or very fat patients the replacement originally may prove very difficult, and on later examinations it may be hard to determine whether the uterus is still in good position. With a stem in the uterus the location of the fundus may be easily determined merely by palpating with one finger the vaginal end of the stem. If the uterus is not in normal position, the stem will prove a great aid in its replacement.

The stem is of decided value in sterility, especially when this seems due to an aplastic uterus. So many factors enter into the question of sterility that it is impossible to determine how much credit should be given the stem when pregnancy follows its use.

A stem pessary may be used as a contraceptive device, but there are other satisfactory and less risky methods available. However, in four patients, for varying periods of time, I have used one for this purpose.

Menstruation is generally regarded as a response by the uterus to the stimulation of certain pituitary and ovarian hormones, and very little is said of any possible reciprocal action upon these glands by the non-pregnant uterus. In abnormal menstruation, good results often follow the administration of these hormones. When a patient with delayed or absent periods becomes regular simply by wearing a stem, the question arises whether this is due to increased production of such hormones from some stimulus arising in the uterus, or does the hormone supply remain unaltered and the uterus, by virtue perhaps of its improved nutrition, now respond to what was formerly an inadequate stimulus?

In considering the use of a stem in a given case, it is of course assumed that any other existing disabilities such as anemia, constipation, obesity, etc., are receiving proper attention, since they are often factors in causing dysmenorrhea. In this connection, endocrines may be indicated even if a stem be used as well.

The ideal case for the use of a stem would be a young nulliparous woman with severe dysmenorrhea, or with scanty, delayed periods or even amenorrhea. Sterility in the married is also an indication. On examination she would show an undersized, movable, sharply anteflexed uterus with no suggestion of cervical or adnexal inflammation, and no history of previous pelvic inflammation. The age is important, for the younger the patient, the more likely is the uterus to resume its interrupted development. A rather similar anatomic condition may be found in hyperinvolution after delivery.

The ideal case, however, is the exception. More often is found, in addition to the anteflexion, an abnormal rigidity of the uterus so that attempts to move it in any direction cause pain. The uterosacral ligaments are specially likely to be involved, particularly when an anteflexion is combined with a retrodisplacement, the condition which Graves calls a retrocession. Without an anesthetic it may be impossible to distinguish this from a retroversion, for the uterus may be so rigid that it cannot be brought up sufficiently far to be palpated properly, and unless the abdominal wall be thin or the patient quite relaxed, the abdominal hand may be unable to feel deeply enough to discover that, although the uterus is far back in the pelvis, the fundus is actually sharply anteflexed.

This rigidity is of the greatest importance, not only in these cases but in almost all pelvic conditions, and yet the textbooks are strangely silent about it and little advice is offered as to how it may be corrected. In fact the rigidity may be a more important factor in causing the disability than the aplasia and anteflexion. Certainly I have effected a cure, or marked improvement, of menstrual pain in some cases by simply mobilizing a rigid uterus. The cause of this rigidity is often obscure. There may be nothing found to suggest an infective origin. In

second, fourth, and sixth month and at this last visit the stem and Smith pessaries are both removed. If there were a retroposition originally, the Smith pessary is left in six months longer, or even indefinitely if the retrodisplacement tends to recur.

As a rule the patient is comfortable within twenty-four hours or less, and in a day or so may carry on her usual activities. Many of the hospital nurses upon whom this procedure was carried out were back on duty three days later. Occasionally, she will have intermittent attacks of cramps which, in most cases, can be controlled by a sedative. They tend to become less frequent and milder until they cease entirely. Very rarely, however, the pain may be so persistent that the stem must be removed.

The amount or duration of the period is usually increased, sometimes so that some styptic, as hydrastis, may be required and rarely the flow may be so profuse that the stem must be removed.

In removing the Smith pessary at each visit the stem may be pulled out with it. This happens very rarely but if so the stem is sterilized and immediately replaced with no difficulty. It may even be possible, in the office, without any anesthetic or dilatation, to replace a stem that had been removed weeks or even months previously.

The full benefit of the stem may not be realized until after its removal, for its presence incites contractions and these may still cause some pain at the period, but rarely as severe as originally.

A permanent anatomic correction of the antelexion cannot be expected, even if the stem be worn for six months. So long as it is in position, the uterus may be perfectly straight; when it is removed the flexion recurs to a certain degree, even if the symptoms have been completely relieved. Apparently nothing but going through a pregnancy and delivery, or having a plastic operation, will permanently correct the flexion anatomically. Probably only occasionally is the dysmenorrhea due to an actual obstruction by the flexion preventing the escape of the menses, for the internal os may be quite patulous and the cramps may be severe for hours or even days before there is any trace of bleeding.

The following results were obtained by the use of a stem pessary, following a dilatation and curetting, in 318 consecutive cases during the fifteen years from 1920 to 1935 inclusive. All were private patients, their histories were taken by me, and they were under my personal care afterward; progress notes were recorded on their histories at every visit.

During this fifteen years, I used a stem in 210 additional cases which are not included in this summary. They represent staff cases in the hospital, a considerable number of nurses in the training school, and a few private patients who married subsequent to the operation and whose histories are filed under their new names and could not be located. The follow-up in most of these additional cases was done by others and the records are not as complete as in the series I report.

In 234 patients, the chief complaint was dysmenorrhea. Of these, 153 or 65 per cent, obtained practically complete relief; 46, or 19 per cent, were partially re-

Three of these, prior to marriage, had already worn a stem to cure dysmenorrhea, with good results. In each case I employed it as a contraceptive under protest and insisted that the patient assume all responsibility for any untoward result. Fortunately none occurred. In this connection, it is of interest that one of my patients, not in this series, became pregnant while wearing a stem to cure dysmenorrhea. The stem was at once removed and the pregnancy proceeded normally for two months longer when she miscarried, apparently due to a bad fall.

A general anesthetic is advisable for the curetting and insertion of the stem. Lately, I have been using evipal intravenously. It operates very rapidly, inducing a deep anesthesia of brief duration, though long enough to carry out the whole procedure. A careful bimanual examination is first made. The pelvic organs should then be thoroughly mobilized by massage and stretching of all the ligaments so that the uterus can be moved freely in every direction and can be brought into perfectly normal position under no tension. In very rigid cases, a large size Hegar dilator within the uterus will aid greatly; with it the uterus may be moved safely and forcibly in any direction at right angles to the long axis of the dilator. The cervix should be very thoroughly dilated. If the internal os be very rigid and narrow, a few shallow radiating incisions in it are helpful. A curetting should be done, for the endometrium may be abnormal and at least it can do no harm. A stem pessary about one-half inch shorter than the total length of the uterus, is then introduced. Many different types have been devised from a simple short piece of glass rod to more complicated forms. My own preference is for a metal stem of the Carstens type, resembling the Chamberlin stem. Both have divergent arms that spring apart within the corpus after introduction to prevent their falling out. However, I always bend these arms close together to facilitate the removal of the stem. With an ante flexion, the cervix is practically always in the axis of the vagina instead of pointing backward as it should. When the flexion is straightened out by the stem, the cervix, being the more fixed part of the organ, nearly always remains in its faulty position while the more movable fundus will be carried backward. The long axis of the stem will then lie in the axis of the vagina, and most types of pessaries are likely to be forced out of the uterus by its contractions. By placing a Smith retroversion pessary in the vagina, the uterus is held in normal position and the vaginal end of the stem lies at right angles to the posterior vaginal wall, which will prevent the expulsion of the stem.

After-Care: The patient usually leaves the hospital the day following the operation. If there is much soreness following the mobilization of a rigid uterus, she may remain a second day and very rarely a third.

She is told to report any unusual pain or bleeding, otherwise to come to my office in two weeks. The Smith pessary is removed at each office visit for an inspection of the posterior fornix for possible irritation. The stem is not disturbed. She is seen again usually at the end of the

for a few very delicate adhesions on the left side, the tube appearing normal. Convalescence was uneventful. The following period was rather prolonged but with only slight cramps. Three months after operation, definite pelvic infection developed and the stem was removed. The inflammation soon subsided under palliative treatment. She was last seen nine months after the operation free of pain but with a slightly cystic and tender left ovary. Later attempts to reach her with letters have failed.

A stem pessary has been used by me in a total of 882 cases, 318 of which are here reported. No examination of the records of the others has been made but I can recall but one serious complication, the development of pyosalpinx two months after the removal of the stem. Probably the stem was not responsible in this case.

The clinical results obtained in this series are comparable with those reported by others. The main purpose of this communication is to emphasize the relative freedom from serious complications in spite of the fact that the stem was used occasionally in connection with an abdominal operation and in many cases that showed definite pelvic inflammation, endometriosis, erosion of the cervix and fibromas all of which are generally considered contraindications for its use.

10515 CARNEGIE AVENUE

ABSTRACT OF DISCUSSION

DR. R. T. LAVAKE, MINNEAPOLIS, MINN.—The value of the stem pessary is so great that we should not allow it to go from the knowledge of our younger men because of any exaggerated fear of its dangers. The results of its use, after every other treatment has failed, are sometimes well-nigh miraculous. Most opinions adverse to the pessary are founded on lack of experience. Many of our outstanding men in evaluating untoward cases that have come to their attention do not seem to have sufficiently considered the improper conditions attending its use in point of pathology and asepsis.

I am quite surprised nevertheless at the frequency with which Dr. Weir, with all his care and conservatism, has felt called upon to use the intrauterine stem pessary. The stem pessary has been the most infrequent type of therapy that I have been called upon to adopt for dysmenorrhea. When I am called upon to use a stem pessary, I always wonder in fact if I have omitted some other form of treatment of less potential danger.

What are the conditions that we should demand before making use of the stem pessary? In addition to eliminating concealed pelvic infection, we should demand a normal cervical and vaginal smear. One condition that I insist upon before using a stem pessary is that there must exist a thorough understanding with the patient that there shall be no intercourse during the wearing of the pessary and no nonaseptic vaginal entrance of any kind. I believe this to be of great importance because, on analysis, in all the untoward results obtaining in the experience of my colleagues and in my observation, this interdiction had not been made or followed.

Dr. Weir's warning in regard to the inefficiency and danger of using the stem pessary as a contraceptive is very timely. It is amazing what intrauterine contraptions are being advertised and not infrequently used for contraceptive purposes.

DR. J. W. KENNEDY, PHILADELPHIA, PA.—For a number of years I had been using the indwelling stem pessary for dysmenorrhea in the undersized hypoplastic uterus with excellent results, but discontinued its use on account of having operated upon two patients for tubal infection who had previously been treated for dysmenorrhea by the insertion of the stem pessary. I now feel that the tubal infection had probably existed before the patient had the stem pessary inserted.

lieved. In 19, or 8 per cent, the relief was not realized fully till after the removal of the stem. No relief was obtained in 16, or 6.8 per cent. A number of this last group had unusual complications such as uterine fibroids, cystic ovaries, etc.

Sterility was complained of in 150 cases, usually with dysmenorrhea as well. Without a complete follow-up, 48, or 32 per cent, are known to have become pregnant. It is impossible to say how much credit is due the stem in these cases, but I think it certainly helped.

Marked irregularity of the periods, from every two weeks to every three months occurred in 19 cases. Of this number, 11 had regular periods for as long as two years after operation.

Seven patients had amenorrhea. One, aged twenty-two had never menstruated but became perfectly regular after the use of a stem. Five had periods of amenorrhea of three to six months and three of these became regular.

The stem was left in the uterus for at least six months in 289, or 91 per cent. In two, the uterus expelled it and it lay free in the vagina. It had to be removed, rarely earlier than one month after operation, in 28 cases, for the following reasons: In 25 on account of excessive bleeding or intermittent cramps, or a combination of both. In one case with local vaginal irritation. In one case it was at once removed when the microscopic examination of the curettings showed some suspicion of early carcinoma, but two years later she was perfectly well and her periods were normal. In two, it was removed for apparent pelvic infection, the only ones showing a major complication in this series of 318 cases.

CASE 1.—J. B., aged thirty-six years, married nullipara, seen first in January, 1920, complained of severe dysmenorrhea and slightly irregular periods. She again consulted me for the same symptoms four and one-half years later. In the interval she had had a curetting by another doctor and this gave her relief for one and one-half years. No history of any previous inflammatory attack was elicited and the pelvis showed merely a small ante flexed uterus. As the first curetting had given such good results, she was advised to have this repeated with the use of the stem as well. This was done one week later, Sept. 29, 1924, at which time a small supposedly follicle cyst was made out in the left ovary. Following the operation, she had a slight rise of temperature but no pain or tenderness until nine days later when she had quite severe pain in the left side. She, herself, pulled out the Smith pessary to get relief and the stem came out with it. Further questioning now revealed a history of an attack of "inflammation" seventeen years previously which subsided under local treatment. A tender mass was now found in the left pelvis, apparently inflammatory but without fever. This rapidly increased in size to the level of the navel and exactly three months after the curetting an abdominal operation was performed, revealing not an inflammatory mass but a papillary cystocarcinoma of the left ovary, the right ovary being normal. Both ovaries were removed. In spite of radium and x-ray treatment, she died more than three years later from metastatic carcinoma of the bladder. The curetting and use of the stem may have stimulated the activity of this cancer but could hardly have caused it.

CASE 2.—R. M., aged twenty-four years, married six months but not yet pregnant, had always had severe dysmenorrhea and scanty periods. In the previous five months she had had two attacks of probable appendicitis with lower abdominal pain, especially on the right, with fever and vomiting. She was distinctly tender over the appendix and the pelvis seemed normal. No infection was found in the urethra, Skene's or Bartholin's glands. Operation July 27, 1921, dilatation and curettage, stem and Smith pessaries, appendicectomy. There were many old and also some recent adhesions between the appendix and cecum and binding the latter firmly to the lateral abdominal wall. The pelvic organs were normal except

RECENT EXPERIENCE WITH A NEW CLASSIFICATION OF PREGNANCY COMPLICATED BY HYPERTENSION AND ALBUMINURIA

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SIX years have elapsed since one of us (F. S. K.) presented to this society a résumé of the 1,100 patients who had passed through the toxemic clinic of the Boston Lying-In Hospital up to 1930, and attempted to correlate our classification of these cases with the Williams-Stander classification.

Criticism by Dr. James A. Davis was impressive.¹ He said both classifications failed to give proper consideration to the medical and pathologic knowledge of the vascular system, including the kidney. Work of others, before and since this time, served to confirm the correctness of this view. Corwin and Herrick and Tillman were in particular convincing.^{2, 3, 4}

In January, 1935, it became possible to reorganize our clinic on a full-time basis, with follow-up facilities. We report the results of observation of patients for eighteen months from that date under a newly arranged diagnostic index which we herewith present.

COMMENT ON CLASSIFICATION

The study of hypertension and albuminuria and their association with cardiovascular and renal disease has revealed certain specific etiologic agents, but many of the causative factors are still unknown. This would appear particularly true as regards those processes which produce permanent vascular damage. It is a natural supposition that pregnancy may play such a rôle. One may say this for two reasons: First, hypertension with or without albuminuria is more common in the female than in the male; the ratio has been reported as high as 3:1. Second, hypertension and/or albuminuria are complications encountered in 5 to 10 per cent of all pregnancies. In an effort to determine the effect of hypertension and albuminuria of pregnancy upon preexisting vascular or renal disease, or the ability of the former to initiate such processes in a hitherto normal individual, one must divide "toxemic" patients into two main groups.

The patient does not experience the painful menstrual period on account of the supposed stenosis of the cervix, but the dysmenorrhea is due to the hypoplastic undersized anemic organ. I have previously called attention to the fact that the cervix of the hypoplastic uterus is never stenosed but, indeed, is more patulous than the normal organ and for this reason dilatation does not often relieve the symptoms. Dilatation of the cervix for relief of the dysmenorrhea has in fact a very narrow field of usefulness and may be advised only in those conditions where we are dealing with spasmodic contraction of the cervix. That the uterus does increase in size after the insertion of the stem pessary has been my experience, and is due to the constant effort of the uterus to expel the foreign body resulting in the increase in size and circulation of the uterus and thus a relief to the anemic dysfunction of the uterus.

DR. GEORGE F. PENDLETON, KANSAS CITY, MO.—The obstetrician is accustomed to go to great extremes in the protection of a patient. I am often momentarily discouraged when the Wassermann test has to be done upon a hundred patients before a positive reaction shows up in one. You will probably say, and I agree with you, that it is worth while to catch the one case in a thousand to safeguard life and health even though we saddle a useless \$5.00 charge on the 999 well patients as we must do in Kansas City.

Now here are some 300 cases with very few known infections, but we cannot rule out the possibilities of hidden or latent tubal or uterine infection. If my logic applies to protection of a patient to the thousandth degree with the Wassermann reaction, why does it not apply in the same degree to the stem pessary, with its possibility of reducing the patient to a state of chronic invalidism more frequently than the hundredth degree? Why protect a woman to an extreme degree in one way if you do not expect to carry the same degree of care in all other ways.

DR. WEIR, (Closing).—As was pointed out, an actual obstruction to the menstrual flow in these antelexions of the uterus is seldom a factor in causing the pain, since the cramps may begin hours before there is any suggestion of bleeding, and even when the antelexion is extreme, the internal os may be perfectly patulous. The purpose of the stem is not so much to overcome any obstruction as to induce a better blood supply to a poorly developed uterus.

Forbidding intercourse to patients wearing stem pessaries has never seemed necessary to me, and it would be very difficult to enforce such a rule.

Whether a given surgical procedure should be abandoned because a bad result may occur occasionally, depends upon one's personal viewpoint. Take for instance a patient having considerable pain from a chronic salpingitis, a condition that will not prove fatal. Shall we allow her to continue suffering and advise against an operation because in a series of such patients operated upon, an occasional patient may die as a result of some complication beyond our control, such as pulmonary embolus? Personally I believe the patient should be advised to assume some risk for the prospect of being cured. The only patient in this series who had a bad result that might be charged to the stem, was the one operated upon for a recent appendicitis. In this instance, it seemed to me that, without risk, the severe dysmenorrhea might be cured by inserting a stem at the same time the quiescent appendix was removed. The complication that resulted was unfortunate but not very serious and to offset this bad result are the large number in whom no complication resulted and the outcome was most successful.

TABLE I. HYPERTENSION AND/OR ALBUMINURIA OF PREGNANCY

GROUP A—EVIDENCE OF DISEASE INDEPENDENT OF PREGNANCY 61 CASES		GROUP B—NO EVIDENCE OF DISEASE INDEPENDENT OF PREGNANCY. 491 CASES	
<p>I. Nephropathies associated with arterial vascular disease</p> <p>Essential hypertension</p> <p>Benign form</p> <p>A. Cerebral change</p> <p>B. Cardiac failure</p> <p>C. Renal failure</p> <p>Arteriosclerotic kidney with uremia</p> <p>Malignant form</p> <p>A. Necrotizing arteriolitis</p> <p>Uremia</p>		<p>I Preeclampsia Grade I</p>	
<p>II. Inflammatory Nephropathies i.e., Nephritis</p> <p>Glomerulonephritis</p> <p>Diffuse</p> <p>Acute</p> <p>Chronic</p> <p>Focal</p> <p>Pylonephritis</p> <p>Acute</p> <p>Chronic</p>		<p>II Preeclampsia Grade II</p>	
<p>III. Degenerative Nephropathies i.e., Nephroses</p> <p>A. Chemical poisoning</p> <p>B. Bacterial toxins</p> <p>Special types</p> <p>A. Amyloid</p> <p>B. Lipoid</p>		<p>III Eclampsia</p>	

Group A: Those patients with evidence of cardiovascular or renal disease prior to the onset of pregnancy. Such evidence is *conclusive* if established before the onset of pregnancy. It is *presumptive* if hypertension and/or albuminuria are present before the twentieth week of pregnancy.

Group B: Those patients who present no evidence conclusive or presumptive of cardiovascular or of renal damage prior to the onset of and through the twentieth week of pregnancy. By this definition, it is seen that we regard albuminuria or hypertension appearing for the first time in a patient after the twentieth week of her pregnancy as resulting only from her pregnant state. Exceptions to this arbitrary division occasionally occur.

We have elected to index cases in which there is conclusive or presumptive evidence of a disease independent of pregnancy (Group A) under the classification as proposed by Fishberg.⁵ Modifications are necessary to make it suitable to the pregnant state. The following groups, in order of frequency, are to be considered (Table I).

Group A: I. Nephropathies Associated With Arterial Vascular Disease.—Many of the cases of hyperpiesis seen in pregnancy are nothing more or less than essential hypertension. The latter occurs in the benign and malignant forms. The former is characterized by the presence of systolic and diastolic blood pressures above normal in the absence of positive urine findings or renal impairment. It occurs more often in patients with positive family histories of hypertension, and also with increasing frequency after the third decade of life. The heart may or may not be enlarged. Arterial pathology can best be demonstrated in the retina as shown by slight caliber changes to definite retinal vessel sclerosis. Such patients carry their hypertension over a period of years and may succumb to cerebral hemorrhage, cardiac failure, or rarely renal insufficiency. The *malignant* form occurs infrequently. Those patients reveal many of the above findings, and in addition, show rapidly progressive hypertension associated with necrotizing arteriolitis which is clinically manifested by typical changes in the ocular fundi and *rapidly* progressive renal decompensation. This form tends to occur in younger individuals than the benign type. Since this is so, and because of its prognostic significance, further experience may demonstrate this to be an extremely important group for study.

In the hypertensive group of patients who are allowed to continue with pregnancy, certain individuals will show increasing hypertension and albuminuria with or without symptoms. Whether this is superimposed preeclampsia is difficult to say. Also, there is the occasional patient in this group who may present other features associated with hypertension, i.e., hypertensive encephalopathy or even uremia with associated convulsions or coma. Such patients are on occasion mistakenly diagnosed as eclamptics. Cardiac failure is encountered, but is rare.

to the appearance of the "pyelitis" an infection of the true kidney parenchyma, which results in permanent renal damage. In the *acute stage* of pyelonephritis, the clinical course may simulate severe pyelitis with or without renal failure which is usually transient. The amount of permanent kidney damage is quite variable as the disease enters the *chronic stage*. Here the differential diagnosis from chronic glomerulonephritis is difficult. The presence of infectious elements in the urinary sediment in chronic pyelonephritis in contrast to the meager or absent hematuria is most important. Pyelography may be of some assistance. The routine kidney function tests and blood chemistry are of value to determine the amount of kidney impairment.

III. *Degenerative Nephropathies*, i.e., nephroses, are characterized by marked edema and albuminuria with absence of hypertension and hematuria. Certain definite causes are many times present, as chemical poisoning, bacterial toxins, obstructive jaundice, etc. In the presence of such known facts a diagnosis of nephrosis is tenable. There are special forms of nephrosis, such as the amyloid type, usually associated with long-standing suppurative processes. Lipoid nephrosis is also encountered, but is rare in adults.

Eclampsia is classified by many as a special type of nephrosis. However, with the clinical evidence at hand and the rather clear-cut pathologic picture, we must believe for the present that the disease is peculiar and related only to pregnancy. For classification purposes, we have removed it from the nephroses and given it a separate entity in Group B.

We believe that the diagnosis of nephrosis during pregnancy is an extremely hazardous one. Certain findings in this disease may be found in the normal pregnant patient, namely, high cholesterol values with lowering of the serum proteins of the blood and the occurrence of doubly refractive lipoid bodies in the urine. It would appear that until knowledge has increased, one should separate into two groups patients who present this clinical picture of marked edema and albuminuria without hypertension or evidence of renal failure:

1. Those patients who present such a picture prior to the twentieth week of pregnancy should be considered as having chronic glomerulonephritis without renal failure, or perhaps, chronic glomerulonephritis with a nephrotic syndrome. As we have previously stated, we believe it is not unlikely that there is an occasional patient with minimal or subclinical chronic glomerulonephritis who, when exposed to the added load of pregnancy, may present such a picture.

2. Those patients who develop such a picture after the twentieth week of pregnancy may be called mild preeclampsies, i.e., preeclampsia Grade 1.

The differential diagnosis in these borderline patients is difficult and at times impossible. Only in the follow-up of such patients can the final and correct diagnosis be made.

Group B: We have further elected to index those cases in which there is no conclusive or presumptive evidence of a disease independent of pregnancy, as heretofore defined, as follows: Preeclampsia Grade 1, preeclampsia Grade 2, and eclampsia.

II. *Inflammatory Nephropathies, i.e., Nephritis.*—Here one may encounter a definite prepregnancy history of acute or subacute glomerulonephritis, or perhaps a story of "kidney trouble" following an acute infectious process. Such patients show edema, albuminuria, hematuria, and hypertension which may occur together or alone. These may be persistent or transient. Renal function is not infrequently impaired, but may be compensated. The urinary sediment usually contains casts and red blood cells. Severe cases may show progressive renal failure with nitrogen retention, vascular damage, and characteristic changes in the ocular fundi.

There are two types, focal and diffuse:

A. The focal is rarely complicated by the pregnant state. There are several etiologic agents such as the emboli of bacterial endocarditis and the glomerulonephritis associated with certain septic processes. The absence of hypertension and edema is characteristic in these cases.

B. The diffuse type may be acute or chronic. The former may occur incidental to pregnancy, but is, no doubt, rare. The chronic phase is more commonly encountered as a complication of pregnancy. Whether the diagnosis during pregnancy is acute glomerulonephritis or an exacerbation of the chronic phase is at the time academic and of little clinical significance as regards the immediate treatment.

Since the chronic form may present varying amounts of renal damage with exacerbations of renal insufficiency, it gives rise to many diagnostic difficulties. This is particularly true if the patient is first observed after the twentieth week of pregnancy. Many patients with this disease have completely compensated renal function. However, the added load of pregnancy may produce varying degrees of kidney failure. The more severe forms are usually recognized early in pregnancy and appropriately treated. However, patients with minimal or subclinical chronic nephritis may not show evidences of renal insufficiency until after the twentieth week of pregnancy. In these patients the differential diagnosis between chronic glomerulonephritis and preeclampsia appears to us on occasion to be impossible as the problem now stands, because all of the kidney function tests are of value only in the presence of moderate or severe renal insufficiency. The actual measurement of kidney reserve would be of aid. If the correct diagnosis could be made during pregnancy, it would be extremely valuable for the intelligent handling of such patients. Only in the follow-up of these patients can the ultimate diagnosis be made.

It is our impression that the milder types of chronic glomerulonephritis often progress to a successful termination of pregnancy. However, we would also emphasize that there is an occasional patient in this group who may for the first time, late in pregnancy, show severe renal insufficiency with uremia associated with convulsions and/or coma. That such a patient has occasionally been mistakenly diagnosed as an eclamptic there can be no doubt.

C. Under the inflammatory nephritides we would add pyelonephritis, which may occur in the acute and chronic form. From many sources^{6, 7} attention is being called to this type of kidney pathology. It is a neglected cause of hypertension which is frequently associated with renal failure. As a complication of pregnancy, doubtless, too little attention has been paid to it in the past, and we would emphasize the need for more careful study of this group of cases with a view to a clearer understanding of the relationship between urinary tract infection and the "kidney of pregnancy." So-called pyelitis is a frequent complication of pregnancy, ante- and postpartum. It seems certain that a number of these patients develop, or have developed, prior

short, and, in many instances, the number of cases reported is too small to do this. The cases represent, for the most part, the initial diagnoses. The final and correct diagnosis has ultimately to be made in these patients.

The total number of cases presenting albuminuria and/or hypertension (excluding acute pyelitis) for an eighteen-month period, beginning in January, 1935, was 552. The total number of patients delivered was 5,497, an incidence of slightly more than 10 per cent.

In *Group A* the total number of cases was 61. They were classified as follows: Benign form of essential hypertension 45 cases (Table II); malignant form of essential hypertension 7 cases; chronic glomerulonephritis 4 cases; pyelonephritis 5 cases, including 1 case proved at autopsy. In the benign hypertensive group, the fetal mortality was 33.3 per cent, accounted for mostly by the interruption of pregnancy before viability (Table III). The clinical findings necessary to determine

TABLE II. BENIGN HYPERTENSION—45 CASES, PATIENTS

AGE	PARA I	II-III	IV-V	VI PLUS	TOTAL
Through 20	1	0	0	0	1
21-24	1	0	0	0	1
25-29	3	2	2	1	8
30-34	1	7	0	1	9
35-39	1	7	4	6	18
40 and over	0	3	1	4	8
Total	7	19	7	12	45

TABLE III.* BENIGN HYPERTENSION. INFANTS

	LESS THAN 4 LB.	4-5 LB.	5-6 LB.	6 LB. PLUS	TOTAL	TWINS	TOTAL
Infants born	14	4	4	23	45	0	45
Stillborn	3	0	0	1	4	0	4
Neonatal death	1	1	0	0	2	0	2
Nonviable	9	0	0	0	9	0	9
Per cent mortality	92.9%	25.0%	0.0%	4.4%	33.3%	0.0%	33.3%

*Infants discharged living, 30.

which of these patients should be allowed to continue their pregnancies are not clear in our minds. It would appear, however, that given a sufficient series with proper clinical data (such as kidney function tests, seven-foot heart plates, and examination of the ocular fundi) correlated with the amount of hypertension, one might formulate more definite criteria for continuation of pregnancy without jeopardy to the baby or undue aggravation of the mother's hypertension. In this series, one can say that in the milder type of hypertension the outlook for the infant is good. How often the hypertension is permanently aggravated, we are not prepared to say.

In patients in whom the diagnosis of chronic nephritis, pyelonephritis, and malignant form of essential hypertension was made, the infant mortality was high because of intrauterine death or operative interruption in the early months of pregnancy.

In *Group B* there were 414 cases of preeclampsia Grade 1 (Table IV). There were 409 babies discharged well. The twin incidence was 2.82 per cent. The uncorrected fetal mortality was 4 per cent (Table V).

Preeclampsia Grade 1: Cases with hypertension and/or albuminuria without other symptoms or signs.

Preeclampsia Grade 2: Cases with hypertension and albuminuria together with some or all of the signs and symptoms commonly attributed to the preeclamptic state, i.e., edema, headache, eye signs and symptoms, nausea or vomiting, alterations in metabolism and blood, irritability and/or lethargy and epigastric pain.

Eclampsia: Cases identical with preeclampsia Grade 2 but with convulsions in addition, or occasionally without convulsions when such a patient, dying in coma, shows findings at autopsy identical with those of eclampsia.

Preeclampsia Grade 2 and eclampsia require little comment. They here agree with the present commonly accepted definitions. We have stated our reasons for preferring not to consider them under the head of nephroses. We bear in mind the identical picture of convulsions in eclampsia and in hypertensive encephalopathy, either of acute glomerular nephritic background or of essential hypertensive background. We have seen cases in which on evidence of history, clinical course, and, on occasion, blood chemistry, the eclamptic state seemed superimposed on essential hypertension, on chronic glomerular nephritis, or on chronic or acute pyelitis or pyelonephritis. Because of these facts, it seems reasonable to conclude that at times the accurate diagnosis of eclampsia, short of autopsy, is not simple. We believe further careful observation of cases will show the need for combined indexing.

Preeclampsia Grade 1 is a more debatable entity, as we have defined it. It includes many of the so-called "low reserve kidney" cases of the Williams-Stander classification as well as some of those we have hitherto classified as "recurrent toxemia." We have adhered to the term preeclampsia because in our experience any pregnant woman with hypertension and/or albuminuria may rapidly, or more slowly, approach eclampsia. The "low reserve kidney" patient is counted on not to do this. Moreover, follow-up of patients in this group tends ultimately to disclose many as essential hypertensives and some as probable or definite cases of chronic glomerular nephritis. It is in this fact that we have encountered in practice the most decided objection to our definition of this group. A negative history in a patient who is first seen late in pregnancy forces us by our definition to include in this group many cases strongly suspicious of disease independent of pregnancy. We do this and trust that subsequent observation in the present pregnancy, interval follow-up study, and behavior in future pregnancy will permit a correct indexing.

This paper deals with the classification purely as a preliminary report. No attempt is made to correlate the causal relationship of pregnancy complicated by albuminuria and hypertension with initial or subsequent cardiovascular-renal damage. The time elapsed is too

SUMMARY

We present a preliminary report of eighteen months' study of patients passing through the reorganized toxemia clinic of the Boston Lying-In Hospital.

We have used a new classification aimed to be all-inclusive when necessary by cross-indexing (Table I). It has for its primary concept the division of all cases into two great groups: (A) Those presenting certain or presumptive evidence of disease independent of pregnancy; (B) those presenting no such evidence.

Group A is classified on the basis of the Volhard and Fahr classification of the nephropathies, modified to suit our idea of the needs in pregnancy. This is not our original classification,⁸ but experience led us to accept it as most satisfactory.

Group B is the commonly accepted one of preeclampsia and eclampsia (well called the "eclamptic state" to emphasize identity) with a debatable group called preeclampsia Grade 1. We have discussed the limitations of this group.

CONCLUSION

The figures reported above are of little value in themselves because of the small amount of material. It is to be borne in mind that the question of classification of these cases is not only of academic interest, but is of primary importance clinically; not pure eclampsia alone makes up the large maternal and fetal mortality assigned to this group. Which of these patients can be carried through pregnancy with a fair prospect of a baby and without permanent vascular and renal damage is not certain. Every one of us proves this for himself with annoying frequency. We interfere when we should not, and we do not interfere when we should. Our small figures are presented only to illustrate the problems we have discussed. By the end of 1940, we shall have observed 1,800 or more patients under this grouping. Perhaps then we can prognosticate the behavior of each group, and even of an individual case in a group. We emphasize that only by the continuous study of great numbers of cases associated with the autopsy findings from many different clinics under a *universal classification* can we arrive at an approximation of the truth and shift the treatment of these patients, who contribute so great a proportion of obstetric mortality and morbidity, from the level of individual opinion to that of a reasoned rationale based on the multiplied observations of many speaking the same language. We offer this classification, not as perfect and not as original, but as an arrangement for universal and practical use of what seems to us at present the best accumulated thought on the subject.

We wish to acknowledge with thanks great help in the preparation of this paper from Dr. Chester S. Keefer, Thorndike Memorial, Boston City Hospital.

In the severe preeclamptic group (preeclampsia Grade 2), there were 65 patients with 54 babies discharged well (Tables VI and VII). The twin incidence was 12.3 per cent. The uncorrected fetal mortality was 26 per cent. In this group, in many instances, pregnancy was interrupted irrespective of the stage of gestation, to avoid the complication of eclampsia.

TABLE IV. PREECLAMPSIA GRADE I. 414 CASES, PATIENTS

AGE	PARA I	II-III	IV-V	VI PLUS	TOTAL
Through 20	26	2	1	0	29
21-24	75	23	0	0	98
25-29	59	33	8	1	101
30-34	25	37	12	14	88
35-39	4	20	16	30	70
40 and over	0	7	4	17	28
Total	189	122	41	62	414

TABLE V.* PREECLAMPSIA GRADE I. INFANTS

	LESS THAN 4 LB.	4-5 LB.	5-6 LB.	6 LB. PLUS	TOTAL	TWINS	TOTAL
Infants born	4	10	44	356	414	12	426
Stillborn	3	0	2	9	14	0	14
Neonatal death	0	2	0	1	3	0	3
Per cent mortality	75.0%	20.0%	4.6%	2.6%	4.0%	0.0%	4.0%

*Infants discharged living, 409.

TABLE VI. PREECLAMPSIA GRADE II. 65 CASES, PATIENTS

AGE	PARA I	II-III	IV-V	VI PLUS	TOTAL
Through 20	6	0	0	0	6
21-24	11	0	0	0	11
25-29	8	7	1	0	16
30-34	9	3	4	2	18
35-39	0	4	2	3	9
40 and over	0	0	2	3	5
Total	34	14	9	8	65

TABLE VII.* PREECLAMPSIA GRADE II. INFANTS

	LESS THAN 4 LB.	4-5 LB.	5-6 LB.	6 PLUS	TOTAL	TWINS	TOTAL
Infants born	15	13	16	21	65	8	73
Stillborn	6	2	0	3	11	0	11
Neonatal death	4	2	0	1	7	0	7
Nonviable	1	0	0	0	1	0	1
Per cent mortality	73.3%	23.5%	0.0%	1.6%	26.0%	0.0%	26.0%

*Infants discharged living, 54.

There were twelve cases of eclampsia. The babies were of secondary consideration. This resulted in a high infant mortality.

In Groups A and B, there will eventuate patients with persistent hypertension with or without renal damage. Evaluation of the effect of pregnancy upon these patients will depend upon the past history prior to pregnancy, combined with the clinical course ante- and postpartum. Upon this basis only can a true concept be formed as to whether pregnancy initiates permanent renal and vascular damage or accelerates these if preexisting.

*Stander**Kellogg*

I. Low reserve kidney

(Pathologically equivalent to nephroses)

Hypertension, moderate, disappears in puerperium

Albuminuria, moderate, up to 2 gm. per liter. Disappears within 3 weeks following delivery

Not aggravated by, or not appearing in, subsequent pregnancies

Blood chemistry and urinalysis negative except 2 above

Edema variable

(Peckham, with Stander's approval, has recently redefined this condition making it conform more closely to mild pre-eclampsia.)

II. Nephritides:

Diffuse glomerulonephritis

Edema, variable, may persist through or beyond puerperium

Albuminuria, relatively severe, occurs earlier in successive pregnancies, may persist between pregnancies

Oliguria

Hematuria

Sometimes visual disturbances

Hypertension, relatively severe, occurs earlier in successive pregnancies, may persist between pregnancies.

Casts

Disturbed urinary N partition, plus Ammon N—Less Urea N

Blood N retention, both urea N and N.P.N.

History

Antedating first pregnancy.

Appears first between pregnancies.

In either of which case some causative factor other than pregnancy may be recognized, or appear to depend only on repeated pregnancies

Low urea clearance

Disturbed relation

Blood urea N to blood N.P.N.

Increased uric acid in blood

I. Degenerative nephropathies (nephroses)

Hypertension absent

Albuminuria marked

(Nephroses a hazardous diagnosis; these cases probably properly assigned to either—

a. Minimal subclinical glomerulonephritis, or

b. Mild (grade I) pre-eclampsia

Edema marked

II. Nephritides

Diffuse glomerulonephritis

Edema

Albuminuria

Hematuria

Hypertension

Casts

Believes none of the kidney function tests are of significance except in the presence of moderate or severe insufficiency, so do not lend themselves to the differentiation between low-grade glomerulonephritis and preeclampsia.

Recognizes the same varieties of history as Stander, and partly bases his classification thereon.

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19 BAY STATE ROAD

ABSTRACT OF DISCUSSION

DR. GRANDISON D. ROYSTON, ST. LOUIS, MO.—If all patients could be seen from the beginning of pregnancy, in most instances those who develop albuminuria and hypertension during this early period could be classified as having had chronic kidney impairment. Likewise, it is logical to assume that those developing signs and symptoms after the twentieth week are due to pregnancy per se. There may be exceptions to this rule, but from our experience in the toxemic clinic in St. Louis, we feel that such exceptions are rare.

In the matter of low reserve kidney, we also prefer to classify such cases as mild forms of preeclampsia. Since the signs and symptoms of so-called low reserve kidney frequently develop exacerbations during pregnancy, the importance of this condition should not be underestimated.

Nephrosis in pregnancy is to be considered, and well-reported instances of lipid nephrosis are found in the literature, but these are rare. Normal pregnancy itself tends to simulate nephrosis, and more so the condition known as hydrops gravidarum of Zangemeister. Furthermore, it must be remembered that Fahr classified the lesion of the kidney, preeclampsia and eclampsia, as glomerular tubular nephrosis, the lesion in the tubules being no different from that observed in nephrosis. The glomeruli show similar involvement. This is true in no other disease. The only marked difference between preeclampsia or eclampsia and nephrosis is that marked hypertension usually exists in the former. The past history is helpful in the diagnosis of nephrosis.

In differentiating cases of chronic kidney disease from preeclampsia and eclampsia, like Stander, we have made good use of the phenolsulphonaphthalein, urea clearance, and creatinine tests.

The much greater frequency of essential hypertension in women than in men is probably due to changes in the renal arterial tree. It is well known that hypertension produces changes in the intima outside the pregnant state. The uterine vessels are peculiarly prone to these changes with prolonged hypertension in pregnancy. The kidney vessels may be affected as are those in the uterus, and this may explain how much of the arterial damage to the kidney can originate in hypertension arising in the pregnant state. Pyelonephritis is a disease in itself, and on these grounds should not be considered in the classification of the toxemias of pregnancy.

DR. S. A. COSGROVE, JERSEY CITY, N. J.—The necessity for one universally used system of classification is to have a valid basis for comparison of nation- or world-wide results which will eventually point the way to universal best management. Unfortunately, we do not yet appear to have arrived at such a satisfactory classification. To demonstrate this I have attempted a parallel comparison of portions of the Stander and Kellogg classifications.

DR. PAUL TITUS, PITTSBURGH, PA.—One difficulty in all attempts at classification of toxemias of pregnancy is met in the names applied to these various manifestations of toxemia. Everyone has been obliged to classify them on the basis of names derived from the symptomatology. Thus we speak of vomiting of pregnancy, acute yellow atrophy of the liver, and eclampsia. As a matter of fact, there are a great many who believe that all types of toxemia of pregnancy are related and that the symptoms vary only as the result of several influencing factors, such as the period of gestation, rapidity of onset of the illness, and the patient's predisposition.

DR. KELLOGG (Closing).—An association for the study of these conditions would result in the development of a universal classification, acceptable to all clinics, so that by mass study we could compile comparable statistics to enable us to know how best to conduct such cases. Not only eclampsia gives a grave mortality but cardiovascular nephropathies associated with pregnancy contribute greatly to a high ultimate death rate.

An example of the problem is the following recent case of mine, a young woman with a blood pressure of 140/100, whom I tried to carry through pregnancy. At the thirtieth week she had a blood pressure of 260/160, heavy albumin, edema, eye symptoms, etc., and a pediatrician advised me that the baby was better out than in. I did a cesarean section and the baby died within thirty-six hours. The mother, four months later, is running a blood pressure of 170/118 and is having cardiac symptoms. Whether we should try to carry patients through pregnancy when they have essential hypertension, and if so which ones, is a thing we can only find out by some mass study.

The question of pyelonephritis associated with pregnancy is of the greatest importance and deserves a much further careful study. We believe that rather a high percentage of patients that we see in pregnancy with so-called "pyelitis" have pyelonephritis. By this we mean infection of the kidney parenchyma. We are indebted to Dr. Keefer of the Boston City Hospital for emphasizing this and making keener our observation of these patients. We think many of these patients die much before their time as a result of being carried through pregnancy successfully.

Owen, Seward E.: The Reaction of Fish to Sex Hormones, *Endocrinology* 20: 214, 1936.

Fish of the bitterling species (*Rhodeus amarus*) were employed in the assay of various concentrations of the prolans, theelin, theelol and antuitrin-S. The results indicate that the female bitterling is refractory to solutions containing these endocrine substances up to 50 M.U. per liter of aquarium water. The male bitterling, while reactive to solutions of these endocrines at concentrations of 0.5 M.U. per liter of aquarium water and more, gives inconstant results.

It is not believed that fish would accurately supplant mice in a quantitative Aschheim-Zondek assay as is employed for teratoma patients. Approximately 75 per cent of fish show positive assay findings when urines from pregnant women are employed.

To avoid the possibility of antihormone interference, animals should not be used repeatedly in assaying hormones.

J. THORNWELL WITHERSPOON.

Retinal changes of rather indefinite significance

Characteristic changes observed by capillary microscopy

Glomerulonephritis may be—

Acute

Chronic

Considers these conditions only in relation to low reserve kidney, nephritis and eclampsia, not as separate toxemia entities

Not recognized as separate toxic entity

This group not recognized as an entity.

Recognizes acute form but questions whether the acute is a primary condition or an exacerbation of chronic form.

III. Nephropathies

Associated with arteriovascular diseases

Essential hypertension

Benign

Malignant

IV. Pyelonephritides

Acute

Chronic

Latter difficult to distinguish from chronic glomerulonephritis

V. Preeclampsia

“Grade I”

Cases with either hypertension, edema, or albuminuria, or any combination thereof, occurring after twentieth week of pregnancy, but *without* signs of renal failure.

The discrepancies between these classifications are apparent. Dr. Kellogg's inability to accept as satisfactory the Stander system is evidenced by his attempt to provide a better one. On the other hand, his frank discussion of the difficulty of allocating many cases in conformity to his own system exhibits his dissatisfaction with the latter. This he freely admits in proposing it, offering it only as the best which, from much study and careful observation, he believes has yet been arranged.

The principal divergence of Dr. Kellogg's system from the Stander classification is the tendency to allocate perhaps the majority of “low reserve kidney” cases to either the mild glomerulonephritis or mild preeclampsia group, which certainly is for the welfare of these patients, for it recognizes in them the always present potentiality of more serious disease.

DR. JAMES E. DAVIS, ANN ARBOR, MICHIGAN.—In regard to the terms nephrosis and nephritis there still exists, even among pathologists, an inclination to classify pathologic conditions from a hypothetical basis, rather than to describe the tissue as found at the time examined. Hypothetically it may be true that some infection has existed in the past and that the condition of change in tissue found at the moment is a result of that supposed infection. Yet when nothing but degeneration is present it is much more satisfactory to record the condition as a degenerative change rather than to enter upon the supposition that it is the result of inflammation, for it is just as reasonable to conclude that this degeneration followed a toxic effect rather than an inflammatory one. The term nephrosis can be distinctly understood as designating a degenerative change found at the time of microscopic examination of the tissue.

In a small number (perhaps 15 per cent) labor will fail before spontaneous delivery occurs, due either to a primary inadequateness of the forces of labor, to the excessive resistance of the more marked disproportions, or to various combinations of both.

If labor fails, indicated by a decrease in the duration and frequency of uterine contractions, before dilatation of the cervix is complete, obstetric judgment alone can estimate, in a given case, if delivery from below will be attended by reasonable success or if cesarean section is not the wiser procedure.

With failure occurring after the cervix is effaced, the following technic is advocated for the occiput which is posterior, and for the so-called transverse arrest.

Briefly, after the usual preparation for a forceps delivery, a cephalic application is made, the head brought down occiput posterior until it can be rotated anteriorly below the outlet, the occiput coming forward external to the ascending ramus.

The forceps, when applied, are in the same relation to the axis of the pelvis as they are at the completion of the first maneuver in the Scanzoni operation; that is with opposed pelvic curves.

An ordinary Simpson type of forceps, without axis traction appliances, is used.

The steps in the technic, with an occiput right posterior, are as follows:

1. Time spent in thoroughly dilating the pelvic floor is more than saved in the case of subsequent proceedings.

2. The left blade is applied anteriorly, starting directly under the symphysis with the handle held to the right of the midline and practically at right angles to the floor. The head is pushed back from the symphysis and the blade guided by a finger through the fenestra.

3. When the blade has reached its approximate correct position, the handle is held temporarily to the left to permit room for the application of the posterior (right) blade.

4. The application of the posterior blade begins with the handle held parallel to the right Pouparts, the handle depressed as the blade follows up the hollow of the sacrum. As the blade comes into approximate position, care is taken to keep the handle well toward the right thigh.

5. The handle of the left blade is now brought over to the right and locked with the right blade.

6. The relation of posterior fontanel and sagittal suture to the blade is noted, to indicate a correct cephalic application. Traction is not attempted until a correct application is secured.

7. Beginning traction is sharply downward, in a line as near right angles to the floor as possible, taking extreme care to keep the handles well to the right of the midline. This is necessary to keep the tips of the blades to the left side of the pelvis, i. e., over the face.

If traction is made with the handles in the midline, the blades are thrown over to the right, *toward the occiput*, and if they do not catch under the mastoids will often slip off over the occiput.

FORCEPS TECHNIC IN THE OCCIPITOPOSTERIOR POSITIONS

A. K. PAINE, M.D., BOSTON, MASS.

THE operative technic to be described is based on the theory that delay in anterior rotation, as the head descends in the pelvic cavity, is definitely the result of cephalopelvic disproportion or that pelvic asymmetry which materially diminishes the room in the fore pelvis. In these cases, with the relatively greater amount of room in the posterior pelvis, the law of accommodation necessitates a posterior occiput, that is, descent in the line of least resistance.

Descent continues in this line until the occiput reaches the pelvic floor to rotate anteriorly in or below the outlet.

This mechanism is easily observed clinically in the patients of this type who deliver spontaneously.

Recent x-ray studies of patients in labor, by a variety of investigators, have caused them generally to arrive at this conclusion, as stated by Thoms for instance, "that the persistent occiput posterior necessarily implies asymmetry, pelvic deformity or cephalopelvic disproportion."

The difficulties with which we are confronted in these cases are those attendant on disproportion in all its implications. The posterior occiput is a result, and not in itself the cause, of the difficult delivery.

This operative procedure is based on the further theory that early artificial rotation of the occiput into the lessened area of the fore pelvis materially increases the difficulties of descent, and that the head needing instrumental aid is more easily brought down with the occiput posterior, in conformity with the first theory, that this represents the natural or favorable mechanism in these cases.

It was formerly thought that an occiput posterior almost always necessitated an operative delivery, this based on the theory that this abnormal mechanism was in itself responsible for the delay in labor. Operation was frequently resorted to as soon as the diagnosis was made, and the first object of many of the operative procedures was to secure immediate anterior rotation.

Fortunately, we have come to understand better the underlying pathology, and to realize that spontaneous delivery will take place in rising 80 per cent of those cases, provided the patient has, or is allowed, adequate labor.

In a general way, the problems are those of disproportion. A first essential in their management is the adequate duration of labor, and a long labor is humanely reasonable with present-day increasingly successful amnesia.

PROFESSOR MILES PHILLIPS, SHEFFIELD, ENGLAND.—In the normal-sized pelvis I think the delay in rotation is generally due to a deflexion of the head, a very important factor. When that is recognized, if I may dare again to refer to Dr. Smellie, his method of pressing on the forehead during the second stage contractions gives the delightful experience of feeling that head rotate, to be delivered shortly afterwards.

In cases of occipitoposterior position it is most important to palpate carefully the ischial spines. If they are unduly prominent, the chances of the long rotation are very considerably lessened, and one is thus forewarned and prepared to interfere, by manual rotation or occasionally by podalic version.

All our students are personally taught to use chloroform, and we use it very considerably. Of course, we also use ether and gas anesthesia, but I believe with Dr. Potter that chloroform has at times great advantages. Last year at the Rotunda Hospital, however, a young woman in labor died under chloroform, and the result has been that chloroform is condemned there now. I think that it is a very great mistake to teach men who are going into the remote parts of the country not to avail themselves of chloroform, for they cannot carry gas or use ether by candle-light.

Is scopolamine in large doses much used here? I mean scopolamine given without morphia, $\frac{1}{400}$ of a grain at half hour intervals, for two or three doses, and thereafter repeated as required. I know nothing that will compare with this in giving relief to the patient, and at the same time not causing a fall in her blood-pressure or depressing the fetus. Its use in this way was introduced at the Queen Charlotte's Hospital, London, by Dr. David R. Jennings in 1929.

DR. F. H. FALLS, CHICAGO, ILL.—There is one method of anesthesia which I think is of value in the occipitoposterior position that has not been mentioned today. This is the local infiltration of the perineum. For the last three years we have been using the perineal block with 1 per cent cocaine and four drops of adrenaline to the ounce. We block the pubic nerve and also infiltrate the skin and do an episiotomy routinely. With the patient unanesthetized and during the labor pains, we find that the head will come down and produce a good deal of its own rotation. If then at the height of the pain considerable rotation is produced, one can apply the forceps, prevent retraction of the head, and complete the rotation with the forceps. We have found this of considerable value.

The reason that we do not use chloroform in our part of the country is because we feel that ether is the best anesthetic for the general man to use in all work. We feel that chloroform anesthesia when given by a trained anesthetist is a very good one. If a student has been taught to use ether and uses chloroform in the same way as he would use ether, he is headed for disaster. Therefore, we feel that if one anesthetic is to be given, ether is the safest to administer, and if the general man wants to use other anesthetics in obstetrics, he should take a special course and learn how to use them safely.

DR. PAINE (Closing).—While this paper primarily deals with an operative technic, a point I especially wish to make is that if these patients are allowed adequate labor, the great majority will take care of themselves without a difficult operative delivery.

8. As the head comes through the outlet, a beginning tendency to anterior rotation may be observed, but it is not permitted (beyond the transverse) until the head is actually crowning, at which time descent is sufficient to permit the occiput to be rotated anteriorly external to the ramus.

9. Anterior rotation is accomplished during moderate traction by elevating the handles, the maneuver ending with traction sharply upward, beginning extension and completion of the delivery with the technic of the usual low forceps.

80 BAY STATE ROAD

ABSTRACT OF DISCUSSION

DR. WILLIAM R. BARNEY, CLEVELAND, OHIO.—At the Cleveland Maternity Hospital we believe that posterior positions are in themselves a cause of difficult labor, due to the fact that the head is usually extended when difficulty is encountered.

It naturally follows that if there is any pelvic disproportion, the labor is increasingly prolonged. We also believe that the majority of these cases rotate spontaneously if allowed to remain in labor long enough, but we do aim to conserve our patients and do this by shortening the second stage of labor by correcting this abnormality. It is not our teaching that anyone doing obstetrics should do this, but only one familiar with obstetric surgery. How this should be done depends on the individual operator, and that method is used which renders safety to the mother and child.

In our clinic two methods are usually used: (1) podalic version when the head is high, and (2) forceps rotation and extraction when the head is in mid- or low pelvis.

We differ from the speaker in our forceps rotation, the posterior blade being always applied first; after the forceps are applied the head is rotated in the plane in which it lies, making no downward traction during the rotation. Then downward traction is made to fix the head at the outlet, the blades removed, reapplied as in a pelvic application, and extraction completed.

DR. IRVING W. POTTER, BUFFALO, N. Y.—The posterior position seems to be accompanied by so many bad results and everyone seems to be so afraid of it that it should be changed earlier. We perform a podalic version in those cases with very gratifying results to the patient, the child, and the doctor. Why anyone should take time in the application of two or three pairs of forceps, or the application several times of one pair of forceps, when he can put his hand in and bring out the baby I cannot understand.

I have not heard mentioned at this meeting the use of chloroform in obstetrics, and yet it is the most practical anesthetic that we have. Chloroform is quick in its action and is pleasant to take, the relaxation is complete, the dangers to the child are not as great as with ether or gas when pushed to the point of relaxation, and the patient wakes up more quickly. I do not know why chloroform has been pushed aside, and the schools are so woefully lacking in the teaching of anesthesia.

DR. S. A. COSGROVE, JERSEY CITY, N. J.—I will not disagree with the assertion that the posterior position is dependent on inadequate flexion of the head. Yet any mechanism which results in posterior descent of the head is a result of the attempt of the head to accommodate itself to a particular pelvis and depends on some structural or dimensional inadequacy as between that head and the pelvis.

More than 80 per cent of these cases will be delivered without the necessity of any interference. It seems that we are wrong in accepting an unnecessary degree of artificial interference in proposing to do podalic versions in more than 50 per cent of these cases.

studied the excretion of intravenously injected bilirubin in dogs, determining the pigment in the bile and urine by means of fistulas of the common duct and ureters. He reported that all the injected bilirubin was found in the bile and none in the urine. These observations were confirmed by Vossius⁸ in the same animal and by Beckmann⁹ in rabbits. In man the kidney takes no part in the excretion of bilirubin, provided the blood serum shows an indirect van den Bergh reaction. In the studies of the above mentioned authors, observations were made only on patients showing an indirect van den Bergh reaction; in connection with our present problem, it may be noted that the serum of the newborn always shows an indirect reaction. Although the bilirubin solution which is injected intravenously gives a direct van den Bergh reaction, as soon as it enters the blood stream it is absorbed by the proteins of the blood serum and the reaction becomes indirect, exactly in the same manner as occurs when a solution of bilirubin is added in vitro to serum.⁵ It can be argued that the injected bilirubin may be phagocyted by the cells of the reticulo-endothelial system in the same manner as occurs when foreign pigments are injected into the blood stream. The observations of Kanner¹⁰ are against such an assumption. Studying systematically the reticulo-endothelial system in different types of jaundice, Kanner found that only in cases of complete obstructive jaundice was there any storage of bilirubin within the Kupffer cells; in conditions of partial obstructive jaundice and nonobstructive jaundice he never found evidence of bilirubin storage whether in the Kupffer cells or at any other place in the reticulo-endothelial system. It is thus clear that intravenously injected bilirubin is not excreted through the kidneys, that it is not retained by the cells of the reticulo-endothelial system, and that it is totally excreted by the liver. The rate at which intravenously injected bilirubin disappears from the blood may therefore be employed as a rational test of the ability of the liver to excrete this substance.

The technic employed by the several investigators who have studied the bilirubin excretory power of the liver is essentially the same. After taking a control sample of venous blood, chemically pure bilirubin dissolved in an alkaline medium, usually 0.1 M sodium carbonate solution, is injected intravenously in a dosage of 1 mg. per kilogram of body weight. Venipunctures are then done after five minutes, thirty minutes, two hours and four hours and the icterus index of these samples, as well as that of the control specimen, determined. In adults the bilirubin content of the blood rises rapidly after the injection and seems to reach its maximum in about five minutes. This elevation in blood bilirubin brought about by the injection (icterus index of the five-minute sample minus that of the control) is taken as representing 100 per cent of the injected pigment. In the subsequent samples the elevations in icterus index above the

THE BEHAVIOR OF INTRAVENOUSLY INJECTED BILIRUBIN IN NEWBORN INFANTS

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OF THE several theories which have been advanced to explain the physiologic jaundice of the newborn, one of the most widely accepted is that which attributes this condition to a functional immaturity of the liver. Proposed first by Ylppö¹ and Ada Hirsch,² in 1913, this theory is based on the fact that the blood of all babies at birth shows a high bilirubin content. In contrast to the usual figure for healthy adults, namely, 0.5 mg., or less, of bilirubin per 100 c.c. of serum, the serum at birth averages 1.6 mg. of bilirubin per 100 c.c., often exceeds 2.0 mg. and is rarely less than 1.0 mg. of bilirubin per 100 c.c. of serum. From this fact it is inferred by those who support this theory that the liver of the newborn, because of immaturity, is unable to excrete the excess bilirubin. It is further inferred that this functional immaturity persists for several days after birth, the resultant retention of bilirubin being often so marked that clinical jaundice is produced. When we add to the above considerations the fact that premature babies are particularly likely to develop jaundice, the hepatic immaturity theory of icterus neonatorum seems altogether plausible. However, as we have noted, the evidence supporting it is largely inferential in character and whether the liver at birth is, or is not, able to excrete bilirubin at a normal rate has never been subjected to actual test. Yet this would seem to be the crucial question upon which the whole theory must stand or fall.

In adults the bilirubin excretory power of the liver has been studied by von Bergmann³ and Eilbott⁴ in Germany, and more recently by Harrop and Barron⁵ and by Soffer⁶ in this country. These investigators injected definite amounts of bilirubin intravenously and then estimated the blood concentration of this substance at measured time intervals. After employing the procedure in a variety of hepatic disorders, particularly cirrhosis, chronic passive congestion of the liver, cholecystitis and miscellaneous cases of jaundice, they conclude that the bilirubin excretory power of the liver is the most delicate method so far proposed for testing the functional capacity of this organ. Certainly, as a measure of the particular function of the liver in which we are here interested, namely, its ability to excrete bilirubin, there can be no question of its reliability. As early as 1874, Tarchanoff⁷

mal limit set by Soffer was exceeded, the retention in one case amounting to 13 and in the other to 9 per cent. We are unable to explain these two aberrant cases, but it is important to note that neither of the infants developed jaundice.

Recalling that the dosage used in this series, per kilogram of body weight, was three times that employed in the adult series of Harrop and Barron, the results lend themselves, upon first consideration, to the conclusion that the liver function of these infants is entirely nor-

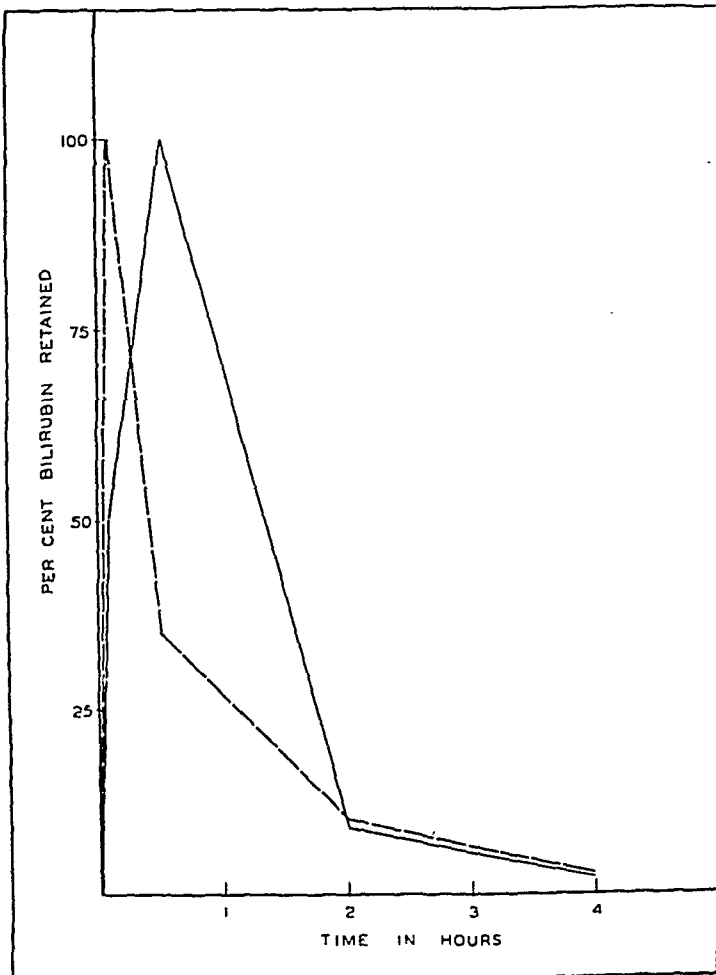


Chart 1.—Showing the average bilirubin excretion curve of twenty-six newborn infants (solid line) and the average curve for adults as reported by Harrop and Barron (broken line).

mal. However, in drawing this deduction we are applying to the newborn standards which are known to be normal for the adult only. The change at birth from intra- to extrauterine existence entails the most profound alterations in physiology, and the first few minutes of life are scarcely a time to apply adult criteria with assurance. In the present study there are several considerations which suggest that some caution must be used in interpreting, without other evidence, the results shown in Chart 1. (1) As we have stated, the dosage used

control level are expressed as percentages of the five-minute elevation. Normally 10 or 15 per cent of the injected bilirubin is retained at two hours, but at four hours little or none is retained. Harrop and Barron, as well as Soffer, base their conclusions on the four-hour specimen and regard a retention of from 5 to 6 per cent at that time as the upper limit of normal. In cases of liver damage from 10 to 35 per cent is still retained at four hours.

The present paper reports a study of the bilirubin excretory power of the liver, by the method just described, in twenty-six full-term newborn infants. In employing this test on the newborn, it was necessary to introduce one important modification, namely, a threefold increase in the amount of bilirubin used. Smaller quantities add a negligible increment to the large amount of bilirubin already present and the relatively slight elevations in icterus index produced by them do not lend themselves to precise evaluation. Accordingly, a total dosage of 10 mg. was used in all babies, or approximately 3 mg. per kilogram of body weight. The chemically pure bilirubin, obtained from the Eastman Kodak Company, was dissolved in 15 c.c. of 0.1 M sodium carbonate solution after the latter had been boiled and cooled to about 80° C. This solution, brought to 38° C., was then injected, with full sterile technic, into the umbilical vein of the infant immediately after birth. Just prior to the injection a specimen of umbilical vein blood was secured as a control and at intervals of five minutes, thirty minutes, two hours and four hours, samples of capillary blood were obtained from the heel of the baby. Icterus index determinations were carried out on all blood samples by the micromethod of Wang and Eastman.¹¹ For reasons which will be explained later, it requires about thirty minutes for the injected bilirubin to reach its highest concentration in the capillary heel blood of the newborn. Accordingly, in the present study, the elevation in icterus index shown by the thirty-minute specimen was considered to represent 100 per cent of the injected pigment. All babies were examined daily during the first week of life for jaundice, and icterus index determinations carried out on the third and fifth days.

The average bilirubin excretion curve of the twenty-six newborn infants is shown in Chart 1, together with the average curve for adults as reported by Harrop and Barron.⁵ Considering for the moment only the right-hand side of the chart, it is at once apparent that the two curves at two hours and four hours are identical. In other words, the injected bilirubin is excreted within two to four hours by these newborn infants as readily as it is by normal adults. The average retention at four hours was 2.7 per cent, a figure well under the normal limit set by Soffer, that is, 5 to 6 per cent. Eleven babies showed no retention at the end of four hours. In two cases the nor-

in the newborn some thirty minutes is required before the capillary blood of the heel shows a maximum saturation with the pigment. As a result the left-hand segments of the two curves are altogether different. This not only introduces a different time element into the newborn curve but raises other questions which are difficult to answer. (4) As we have already stated, the bilirubin content of the blood at birth is normally high. In other words, the blood bilirubin levels before the injection and after the excretion of the pigment are dif-

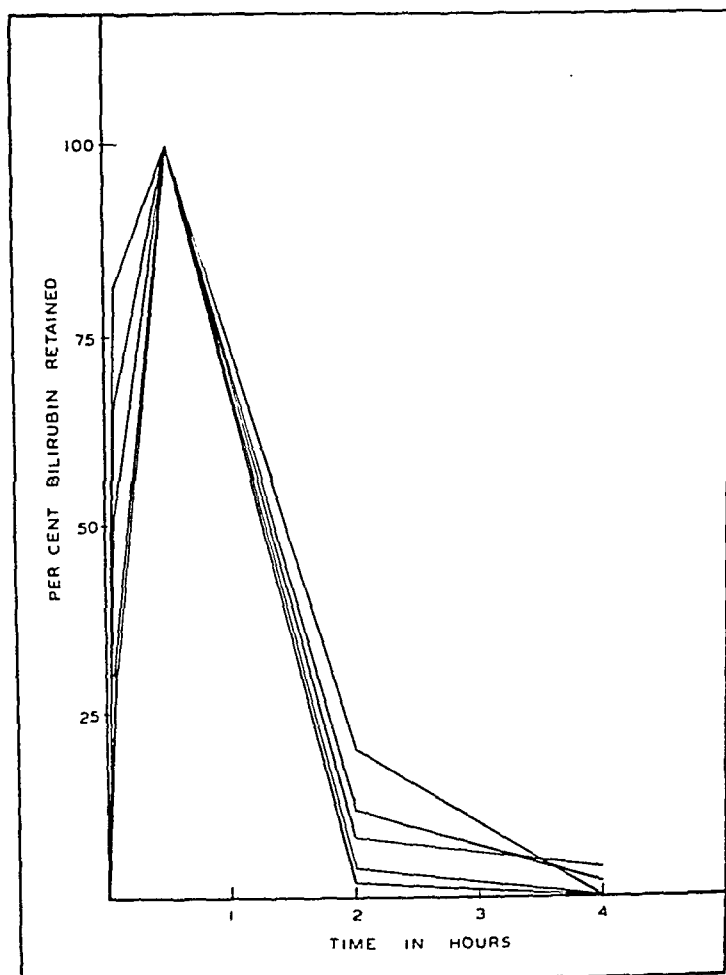


Chart 3.—Showing the bilirubin excretion curves of five infants who *did* develop jaundice. The icterus indices of these babies reached the following levels: 160, 120, 120, 100, 80.

ferent in the two groups. While this would seem to be of little importance it constitutes still another difference in basal conditions between the adult and the newborn.

Since these several peculiarities of the newborn state make it hazardous to apply at this period adult criteria for bilirubin excretion, it would seem more logical to employ as a standard the bilirubin excretion curves of newborn infants who do not develop jaundice, and to compare with these the curves of several babies who later manifest

was three times that employed in the series of Harrop and Barron, and while this fact would seem to render the results all the more convincing, nevertheless it leaves much to be desired when we attempt to compare the two series with any degree of precision. (2) It is questionable whether the relatively great size of the liver in the newborn may not more than offset this threefold dosage; in any event this introduces a factor which it is almost impossible to evaluate. (3) It is well known that the capillary circulation, particularly that in the

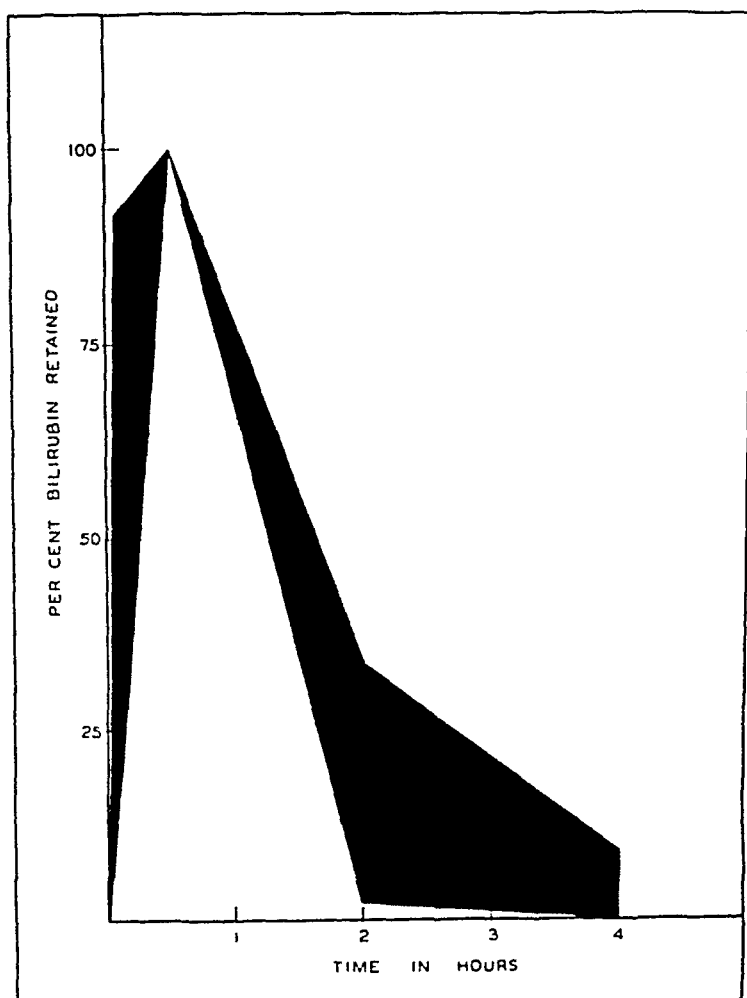


Chart 2.—Showing the composite pathway of eighteen bilirubin excretion curves from infants who did *not* develop jaundice.

extremities, is not well established in the newborn until some minutes after birth. The cyanosis which is commonly seen in the fingers and feet of newborn infants, the first half hour or so of life, is but one evidence of this condition. In the present study, with the exception of the control sample, capillary blood from the heel of the infant was used and the state of the capillary circulation during the first few minutes after birth is clearly seen in the left half of Chart 1. In the adult series the concentration of the injected bilirubin in the venous blood reaches its highest level within five minutes after injection, but

DR. EASTMAN (closing).—The greater part of this work on the bilirubin excretory power of the liver in newborn infants was carried out at the Peiping Union Medical College, Peiping, China, and the technical procedures were done by Dr. Hazel Lin, assistant resident in obstetrics and gynecology at that institution. Her name appears as coauthor on the paper and I wish to make acknowledgment for the large share of the work which she did.

THE ABNORMAL BANDL RING

GEORGE F. PENDLETON, M.D., F.A.C.S., KANSAS CITY, MO.

I PRESENT to you herewith a statistical discussion of the abnormal Bandl ring, but I do not intend to quibble over whose name should receive prior right to that ring. In order to clarify the conflictions in our literature let us recognize two main types of muscular spasms within the gravid uterus.

The "constriction ring" frequently occurs under the name "hour-glass uterus," where it retards completion of the third stage of labor. It is often found as a muscular ring retarding products of conception in incomplete abortions. It occasionally remains even after all gestational products have been removed from the uterus. This ring protrudes inward from the uterine contour like a smooth ridge, gradually rising from its surrounding level to a rounded edge and then as symmetrically curving backward again on the other side. The ascending and descending curves have equally thick muscular walls and shallow concavities. This ring has no definite anatomic location, and it is found at any uterine level from one cornu to the lower portions of the corpus uteri. It is generally circular and can occur in the presence of the other type of ring.

The "Bandl ring" has only one anatomic location, namely, at the caudad end of the muscular corpus uteri. Its base is generally not as wide as that of the constriction ring. The top may be rounded (79 per cent) or blunt (21 per cent). The cephalic curve is similar to that of the other ring but the caudad curve is steep as the thin lower uterine segment falls away from its ridge just like a precipice dropping directly from a mountain top.

The physiologic Bandl ring is present in every labor as an integral part of the normal uterine mechanics while a constriction ring is a distinct abnormality. As long as the normal Bandl ring moderately contracts with and relaxes between uterine pains, it is performing its normal function but when it remains spastic and retards fetal advancement, it has become abnormal.

There are many minor grades of abnormality wherein these rings readily respond to rest, drugs and anesthesia, and these are hard to

icterus neonatorum. Surely, if icterus neonatorum is due to a functional immaturity of the liver, infants who develop this condition should show at birth some impairment in their capacity to excrete bilirubin when compared with a group of babies who do not develop jaundice. Of the twenty-six infants studied five developed marked jaundice between the third and fifth day of life with icterus indices ranging between 80 and 120. Three babies showed questionable jaundice and may be dropped from consideration. The remaining eighteen infants manifested no evidence of icterus neonatorum and their icterus indices showed at no time an appreciable increase. The composite pathway followed by the bilirubin excretion curves of these latter eighteen babies is shown in Chart 2. In Chart 3 may be seen the individual curves of the five infants who later developed icterus. It is at once evident that these five curves fall well within the pathway shown in Chart 2. They tend, indeed, to follow the lower part of this pathway and in three of the five cases no bilirubin was retained at the end of four hours.

Accordingly, whether we employ as a standard the adult bilirubin excretion curve of Harrop and Barron (under differing basal conditions, it is true), or the curve of infants who do not develop jaundice, it is clear from these studies that the bilirubin excretory power of babies who later develop icterus is entirely normal at birth. We are inclined to conclude, therefore, that functional immaturity of the liver is not a cause of icterus neonatorum in normal full-term infants.

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ABSTRACT OF DISCUSSION

DR. PAUL TITUS, PITTSBURGH, PA.—Dr. Eastman and his coworkers have conducted an extremely ingenious investigation of the theory that the immature liver of the newborn infant requires a few days in which to adjust itself to the burden of extrauterine life. They seem to have disproved that theory by injecting bilirubin and measuring the output of the livers of those infants who had become icteric, but nevertheless readily excreted this substance.

There is one clinical point that has attracted my attention. For some time in our clinic we have clamped the cord immediately so that the baby is not permitted to get the extra blood retained in the placenta and cord. It has seemed to us that with this immediate clamping of the cord there has been considerably less icterus neonatorum. Whether this means that the condition is due to the breaking down of excess red blood corpuscles is of course debatable.

Abdominal groove palpation (9 per cent) was unusual. I am of the opinion that the furrow caused by a contracted uterus upon a fetal posterior position after the bag of waters has ruptured has been mistaken for a Bandl ring groove. These furrows merely hug the fetal concavities and are not diagnostic of abnormal rings nor do they occur at the ring site. The real grooves had a narrow tonic base (100 per cent), never very prominent and could not be indented under Mueller's grip.

In my cases cervical dilatation seemingly ceased in the middle of the first stage of labor and after artificial rests slowly and grudgingly reached full dilatation (72 per cent), while 22 per cent attained almost full dilatation. My experience was unusual, for only 6 per cent of the cervixes remained rigid. I am inclined to agree with Harper that the so-called rigid cervix in labor is not due to inherent anatomic defects in that cervix but rather to the improper uterine mechanics for normal effacement.

In this series of cases 92.5 per cent had a vertex presentation. Moderate head extensions (63 per cent) were common and 68 per cent had movable fetal heads at the height of an uterine contraction. Generally the presenting part could not be elevated very far.

Presenting parts retracted away from the examining finger at the height of the uterine contraction in 17 per cent of the cases, and I consider this as diagnostic evidence of an abnormal Bandl ring, but it is not always present. In the presence of an abnormal ring, during uterine contraction, the ring will retract toward the fundus or else the fundus of the uterus will be drawn toward the ring. In the latter case there will be no retraction of the fetal head at the height of an uterine contraction.

I have created a term "station recession" to describe the history of the position of the presenting part which I have observed occasionally ends higher up than at some time previously in the labor (18.9 per cent). While not diagnostic, I consider this observation as a very suggestive sign of an abnormal ring.

I do not agree with those who insist that the level of the fetus signifies the level of the ring. Anatomically the ring is always at the same level. In relation to the maternal abdomen, level depends upon the length of the lower uterine segment, which is easily demonstrated during intrauterine manipulations by the ease with which one can raise or lower this level. I palpated rings at or above the level of the navel in 44 per cent and at the promontory in 45 per cent of the cases. The ring was about the fetal neck in 67 per cent, the body or fetal hips, 3.8 per cent, and once about the neck in a breech presentation.

Many of these rings barely allowed entrance of the fingers between the ring and the fetus (30 per cent) and none had twice that space. Some had no space when they were discovered (18.8 per cent). Only

classify. In my series of 53 cases of abnormal Bandl rings I have disregarded all minor grades of abnormality and describe only those cases which retarded fetal advancement and remained tetanically contracted even under ether anesthesia deep enough to cause wide pupillary dilation. All these cases are taken from my own private practice in white women and have been carefully recorded as they occurred over a period of twenty years.

It is my belief that the obstetric operation is too often glorified while the indication for it is minimized. I believe that the incidence of this ring is hushed under the terms "delayed labor" and "difficult forceps," cases wherein a retarding muscular ring may be more responsible than the lack of descent, flexion and rotation of the fetal head. In 12,000 deliveries in Kansas City hospitals the incidence varied from 0.2 per cent to 0.35 per cent.

My cases had eight noteworthy etiologic factors. In this series 21 per cent of the patients were obese, 58 per cent were overdue by Nägele's rule, 55 per cent were primiparas, 62 per cent had the bag of waters ruptured at or before the start of labor, 58 per cent had a forced labor either by induction or otherwise, 58 per cent had pains too fast and furious for that particular stage of labor, 74 per cent had posterior positions, and last, 57 per cent were consultation cases. In the latter group all the maternal deaths occurred. In view of my postulation that abnormal rings are more common than the texts admit, I sound an added warning to those who routinely rupture the bag of waters in early labor, and I wish to magnify rather than minimize the danger in posterior positions.

All these rings occurred in the first stage of labor and many belonged in the delayed labor group (58.5 per cent). Three labors lasted more than seventy hours.

In the very painful labors (87 per cent) only one patient had agonizing pain, while two others gave very little evidence of pain. In general, pains frequently decreased in intensity and lengthened in interval, and in a few, even returned to complete quiescence for a while during the labor. Morphine, scopolamine, or ether-oil generally controlled them while the barbituric acid compounds did not do as well. I agree with Harper that the characteristic pain is low down in front (90 per cent) and not in the back. Senseless, irregular, unreliable, nagging, short pains, more painful to the patient than her appearance or my palpation would suggest, describe them best.

Uterine contractions were as misleading as the pain and 73 per cent were clonic in character. Often they were jerky in onset, came to a zenith quickly, and faded slowly. My experience does not agree with Harper's, who insisted that the uterus never reached absolute relaxation but had the same tone between as with contractions. The diagnosis is not that easy.

whose bag of waters has ruptured many hours previously, and even after grasping the feet of the fetus the turn was so difficult that on several occasions I have tied gauze to the fetal feet to help make the turn in the version. Generally the ring relaxed when the turn was accomplished and only in a few cases did the ring actually retard the after-coming head. In these cases I applied forceps and pushed the ring backward over the fetal chin. I have always been anxious about the condition of the lower uterine segment, and after fetal extraction I have generally palpated it for ruptures. In the treatment of these cases the best success will follow early recognition of the Bandl ring. I am still of the opinion that severe premature separation of the placenta and abnormal Bandl ring are allowable cases for manual dilatation of a cervix in certain cases, but I cannot agree with Michael who advocates massaging the uterus to relax the ring. In view of my 4 maternal deaths, 15 stillborns, and 5 babies dying in the hospital, I believe that we should advocate more cesarean sections and fewer podalic versions.

The conduct of the third stage was generally routine and easy, but manual removal of the placenta (18.8 per cent) was often done unless complicated by shock (16.5 per cent) or third degree laceration (9.4 per cent). I have never seen an abnormal ring that did not completely disappear within five to thirty minutes after completion of the third stage of labor, which cannot be said of the constriction rings.

Lacerated cervixes (32 per cent) were repaired immediately but never in the presence of shock or third degree lacerations. Blood loss of 500 c.c. occurred in 16.5 per cent and was more frequent in the multiparas (57 per cent). Temperatures of 100° F. or more during the hospital stay were 41.5 per cent and were mostly in the versions (90 per cent). Recovery was generally rapid and pulse rates over 100 occurred in 34 per cent and were mostly of short duration. The usual fourteen-day hospital stay was extended in 15 per cent.

The fetal loss was greater in the males (75 per cent) and also 85 per cent were versions. The 4 maternal deaths were all in difficult consultation cases, all long labors, 75 per cent in primiparas, 75 per cent following podalic versions, and 75 per cent in very obese cases. Two died from shock and hemorrhage and 2 died from sepsis. There were 2 ruptured uteri.

CONCLUSIONS

I have related my experience and opinions concerning 53 abnormal Bandl ring cases which occurred in my own private practice.

I have confessed a serious maternal and fetal mortality with the use of podalic version, and I now urge more cesarean sections.

I have emphasized "station recession" as a diagnostic sign of importance.

two of my cases responded to hypodermics of adrenalin and none relaxed with the use of atropine or ephedrine. I have had no experience with amyl nitrite, the hot tub bath or the hot vaginal douche. I believe that these tetanic rings require long constant pressure under deep anesthesia if they are to be relaxed by intrauterine manipulation.

Diagnosis is absolute only when we feel the ring. It is very sure when the presenting part retracts at the height of an uterine contraction. It is highly suggestive in the presence of station recession. It should be seriously considered when fetal advancement in the first stage of labor ceases or the presenting part is freely movable at the height of an uterine contraction, when we palpate a true ring groove, when progressive dilatation ceases in the presence of pains (90.5 per cent) and when forceps applications do not allow easy advancement of a normally flexed fetal head without other known cause. I have refused to recognize these suspicious signs in 38 per cent and allowed these cases to drift into very difficult problems. It is my observation that many experienced doctors live through a fairly successful medical life with little knowledge of Bandl ring dystocia. They attribute their occasional difficult labors to asynclitism and mild head extensions which their forceps will correct. They resort to unbelievable stresses, tugs, and crisscross pulls upon a fetus whose mother is under deep anesthesia. By a tiring process upon a hidden ring they relax or tear it and deliver dead babies through badly lacerated channels. Certainly when forceps do not easily rotate and extract a fetus, we should be suspicious of retardation by a tetanic muscular Bandl ring.

My general procedure in handling these rings was a trial with forceps or manual rotation of the fetal head. I manually dilated a few cervixes when it seemed necessary. When these procedures failed I palpated the uterus internally for diagnostic evidence of the ring and when found, the anesthesia was changed to deep ether. In the meantime hypodermics of adrenalin, atropine, or ephedrine were tried and with the exception of two cases in which adrenalin was used, these drugs have failed me completely. Under deep anesthesia I pushed my fingers between the ring and fetus. Some cases required much pressure to do this. With my fingers over the ring, long tiring pressure was exerted against the ring, using the fetus as a leverage. This I now believe is wrong and increases the fetal mortality. Occasionally the ring dilated enough to allow the use of forceps and extraction (17 per cent), but generally I was obliged to push the fetal head backward through the partially dilated Bandl ring and perform podalic version (74 per cent).

My experience has been that a dilated ring will always contract some when the pressure of the hand has been removed. A podalic version of itself is not a difficult procedure. It was the indication for which that version was done which caused my troubles. Naturally a podalic version is a difficult procedure in the presence of a contracted uterus

My feeling about these cases is that in many of them there were unnecessary attempts to induce labor, and trouble came from forcing the uterus when it was not ready for labor. The real cause for the occurrence of so many of these abnormal Bandl's rings was in the management of the early stages. Bandl's ring does occur, but it should not occur in carefully managed cases to any such extent as Dr. Pendleton would lead us to understand.

DR. JAMES R. BLOSS, HUNTINGTON, W. VA.—My own opinion regarding the treatment of these cases is that adrenalin does relax many spasms of the uterus. Nevertheless when I find a Bandl ring with such symptoms as described in the paper, it has been an invariable rule with me to deliver that patient by section.

PROFESSOR MILES PHILLIPS, Sheffield, England.—Dr. Pendleton has spoken of the use of deep ether anesthesia, and I would like to ask him the duration of the ether narcosis, because I think such contraction rings may disappear with prolonged ether anesthesia. I have on several occasions seen the rapid and absolute disappearance of the ring with the use of capsules of amyl nitrite broken under the ether mask—two, three, or even more in rapid succession. This method of treatment was introduced by G. R. Croft, of London (*Lancet*, 1928). I quite recognize that there is a certain stage where the disappearance of the ring is impossible and it is found even postmortem.

I would like particularly to speak about the early clinical phenomena which precede the contraction ring. That is the time, I think, when the possibility of the ring should be recognized. The normal time relationship between uterine pain and uterine contraction must first be recalled. The contraction can be felt by the obstetrician's hand before the pain is felt by the patient and, more important still, the contraction only ceases after the pain is over. Of all the textbooks that I have consulted that by DeLee is the only one which mentions this important fact.

When these troublesome, colicky pains are suspected it is always my first step to place a hand on the uterus and ask the patient to explain the exact sort and the duration of the pain she is experiencing. Sometimes the pain is very excruciating and it is usually confined to the lower abdomen, often only on one side, for the abnormal contraction more often produces a shelf than a complete ring.

Another important point is that the patient often strains and struggles with this colicky contraction of the uterus and the attendant may be led to think that she is in the second stage.

DR. PENDLETON (closing).—The statement that these cases were mismanaged I certainly agree with and it was my purpose to show this. Many of these were, however, consultation cases. Thirty cases were forced labors, 35 were unsuspected and 38 had tonic uteri. We should have been bolder and interfered earlier. Of the 30 cases of forced labor, 9 received quinine, either alone or with castor oil, while 2 were given two or three minims of pituitrin. We feel that all of those cases were mismanaged. Thirteen of them also had bags and 12 had some other form of attempt to force labor.

I have never carried a patient under ether long enough to show whether the ring would finally relax. The moderate ring will readily relax under adrenalin, but I have had little success with adrenalin in the type which I have described.

The usual statistics are not favorable to podalic version, although I did say it was not a difficult procedure. I did not say it was safe or desirable. All I said was that it was the indication for which the version was done that caused my trouble.

I question the advisability of too fast and furious pains in early labor, the use of hypnotics rather than uterine relaxants during labor and the early rupture of the bag of waters to hasten delivery.

From experience I doubt the value of adrenalin in relaxing these serious rings.

Last, I have called attention to eight salient predisposing factors in my cases which were indirectly responsible for superirritable uteri and abnormal Bandl rings.

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ABSTRACT OF DISCUSSION

DR. ROBERT L. DENORMANDIE, BOSTON, MASS.—When a complication giving a 7 per cent maternal mortality and a 37 per cent fetal mortality occurs, it deserves our closest consideration. I fully agree with Dr. Pendleton that there is such an entity as Bandl's ring, and that at times it is a serious complication. I do not, however, agree with him that what he calls his eight "salient features" are the cause of this ring. If excessive gain in weight during pregnancy is a cause, if primiparity is a cause, if early rupture of the membranes is a cause, if too severe pains for the state of the labor or posterior positions are causes, then I am confident that I should have seen many more of these abnormal Bandl's rings in my own practice than I have.

I was at a loss to understand why Dr. Pendleton met so many of these cases, and I therefore asked him if he would send me an abstract of his cases. In analyzing these cases I think the explanation of why he had so many abnormal rings is clear. Dr. Pendleton puts, in my opinion, too great stress on the patient being overdue. He constantly attempted to start the patient up with castor oil, and if that was unsuccessful he often put in a Voorhees' bag. Many of these cases, I believe, were not ready for labor, and it is a well-recognized fact that a uterus that is irritated oftentimes will not properly contract. Again, there were cases of primiparas where the head was high, and they were allowed to go into labor for a long while with no descent. Disproportion was present and they should have been managed differently. Pituitrin was given before full dilatation. Again and again the patient was allowed to stay in labor with full dilatation for many hours, and in one case the head was in sight for four hours. Again, I do not think it is good obstetric practice to allow a patient with ruptured membranes to be up and around the hospital, leaking fluid constantly, or to be sent home with ruptured membranes. The probability of the uterus becoming tetanically contracted is great. Again and again these patients showed slow, nagging uterine contractions with no effect on the cervix, and the question comes to mind, were these patients in labor at all? Would it not have been ever so much better to have given them a good sound sleep and not to have irritated the uterus by castor oil and by putting in a large Voorhees' bag?

Dr. Pendleton states that, "A podalic version is not a difficult procedure," but that it is the indication for the version which causes his troubles. I disagree with him totally in that statement. How he can say it is not a difficult procedure in the face of severe tears, four of which were third degree, ruptured uteri, and his high maternal and fetal mortality, I cannot understand. In my opinion a version in a tight Bandl's ring is one of the most serious, difficult procedures there is in obstetrics.

lationship to nasal allergy. In this rather detailed review of the causes of essential dysmenorrhea, no mention is made of the relationship of allergy to this condition.

References in the literature concerning the relationship of allergy to essential dysmenorrhea are very scanty, and so far as we are able to make out there are no detailed references. Duke, in his monograph on asthma and allergy, makes a statement concerning the disturbances of menstruation with allergy. He has rather frequently observed patients having symptoms as a result of general reaction. He states that a wide variety of symptoms observed in these cases have disappeared after appropriate treatment. In one food sensitive case, menstruation which had been not only extremely painful but had occurred twice monthly for years, became completely normal and occurred at four-week intervals upon the avoidance of foods to which the patient reacted.

Cooke says dysmenorrhea or rather untimely and scanty menstrual flow following acute cramplike pains in the lower abdomen is recorded in two women twenty-six and thirty-eight years, respectively. In both of these cases, Cooke states, the symptoms were part of an immediate reaction with asthma, coryza and urticaria, the menstrual flow itself not being apparent until three hours later and lasting one day.

Rowe, in an article on food allergy, confirms the opinion of Duke that menstruation can be disturbed and may be irregular and painful by food sensitization.

The statement of Duke that the patient had been relieved of all pain at the menstrual period following dietetic treatment of allergy, impressed us very much. It has been known that the uterus of the guinea pig is the most satisfactory tissue to use in determining the relative potency of test allergies. As we had the opportunity of studying a good many patients with essential dysmenorrhea, we thought it would be interesting to try out his idea. As previously stated, the first report consisted of twelve complete cases. The patients complained of three symptoms: dysmenorrhea, mucous vaginal discharge and irregular menstruation. All were nulliparous women, ranging from eighteen to thirty-four years of age. They were under observation for from three to eighteen months. The dysmenorrhea complained of had existed for varying periods of years; in some since onset of menstruation, in others it came on well after the period had been established. The mucous discharge varied from just a noticeable amount to that demanding a napkin be worn constantly. The irregularity of menstruation varied from six weeks to six months. The occupations of the patients were stenographers, college students, and two were unemployed.

ESSENTIAL DYSMENORRHEA AND ALLERGY

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IN 1926, while physician to students at the Washington University, several cases of essential dysmenorrhea came to the attention of one of the writers (Smith). It was felt that some form of allergy might be playing a part in bringing about these symptoms. While this work was going on, and several interesting cases had been observed, it was found that Duke, in his monograph on asthma and allergy, had made reference to this subject. The work was continued, and in 1931, twelve cases were reported, eight of which received complete relief, and four partial relief after the causative agents were eliminated from the diet. It might be of interest to review here some of the points that were brought out in this preliminary report.

According to Graves, essential dysmenorrhea is a disturbance that is characterized at the time of menstruation by severe cramplike pains in the lower abdomen from which the patient is entirely free during the intermenstrual period. He points out that this form of dysmenorrhea is distinctive and must not be confused with the kind of menstrual pain resulting from aggravated menstrual congestion, complicated by various pelvic disorders, particularly salpingitis and other pelvic inflammations. To the latter type the term secondary or acquired dysmenorrhea is given. Graves mentions that essential dysmenorrhea is one of the most common gynecologic diseases, but comparatively little is known concerning its etiology. In discussing the etiology, he tells us that the old authors regarded the cause of dysmenorrhea as entirely mechanical. Other writers divide dysmenorrhea into three classes: an organic form, depending on obstruction, a congestive and a neuralgic form. Graves states that Schroeder thinks there may be an excessive irritation of a vegetative nervous system by toxic substances that the function of menstruation evokes in the blood. This theory is supported, Graves suggests, by the relief that is often secured from the administration of atropine. He also mentions the so-called nasal dysmenorrhea which has been described by Fliess and elaborated by Schaeffer. Pains of dysmenorrhea have entirely disappeared by the application of cocaine to the tuberculum septi of the nose, which is designated as the genital spot. This is interesting to mention, because one of the cases of dysmenorrhea which was cured, was found in re-

lieve most of these reactions would be considered doubtful or negative by those accustomed to seeing the tremendous wheals and areas of erythema that have been mentioned so frequently in children and some asthmatic individuals.

In our series, the foods most frequently giving positive reactions were wheat, eggs, milk, chocolate, fish, beef, pork, nuts, beans, pepper, cabbage, cauliflower, etc. We were impressed that in so small a series, five patients had had abdominal operations and three dilatation and curettage because of dysmenorrhea, and that none had experienced more than temporary relief by these operative procedures. We mention, without knowing the significance of the fact, that three became pregnant after being on the diet a very short time.

Upon further study of the nine cases that gave only partial relief to allergic treatment, by adding thyroid extract to our treatment, two of these immediately became completely relieved. If the diet was broken and the thyroid continued, they dropped back into the group of partial relief. There was one other case that by the addition of lutein substance became a complete relief. In the six cases that were recorded as no relief, one experienced partial relief by taking thyroid, and two others were considerably relieved by taking emmenin and continuing their diet. We mention this additional therapy because we are definitely of the opinion that allergic dysmenorrhea is often combined with endocrine manifestations, pelvic inflammation, malpositions and tumors.

The complete cures are very striking indeed as illustrated by the five following case reports:

CASE 1.—M. D., aged twenty, college student. Has hay fever spring and fall. Known to be sensitive to oak and ragweed pollen. Operated five years ago, appendectomy and right oophorectomy, slight relief. Physical and pelvic examinations negative. Menses, onset fourteen years, every ten days to eight weeks. Pain at menses began about one year after onset of periods. Pain for one full day, frequently for two or three days. Marked nausea. No vomiting. Moderate amount of mucous vaginal discharge. Has noticed abdominal pain or discomfort and nausea after eating fish, oysters, shrimp, cabbage and cranberries. Positive skin tests were obtained to fish, milk, eggs, chocolate, beans and peas. On eliminative diet. Free from pain for six consecutive months. Was exposed to excessive pollen, followed by rhinitis, coryza, and painful menstruation after ten-day interval. Again free of pain for four months while on diet until exposed to ragweed, followed by rhinitis, coryza, and severe dysmenorrhea with menstruation at fourteen-day interval. Next five menses at regular interval and free of pain, diet had been continued.

CASE 2.—E. L., aged twenty-four years, housewife. Married three years. No pregnancies. Severe cramps first day of menstruation. Always nauseated. Usually vomits. Severe mucous vaginal discharge. Menses, onset 13 years, every 28 to 30 days and lasts four or five days. Onset of dysmenorrhea four years ago. Physical and pelvic examinations negative. No family or personal history of allergy. Scratch skin tests were mildly positive or questionable to most foods. Patient was put on

Since this report, 35 additional patients have been treated with complete relief in twenty, partial relief in nine and no relief in six. It is interesting to note in this series of cases that 32 were nulliparous and three were multiparous. Their ages, at the beginning of the study, varied from fifteen years for the youngest to thirty-four years for the oldest. They have been under observation for periods of from six months to five and one-half years. In some the symptoms began with the onset of menstruation, but in others the difficulty came on many years after the menstruation had been well established. The irregularity of the menstrual periods varies tremendously, from intervals of six days to intervals of three and four months. The mucous discharge existed from just a noticeable amount to amounts demanding that a napkin be worn almost constantly. The occupations of this group were clerks, stenographers, college and high school students, nurses, housewives, and unemployed. After this study was begun, it was found that a careful and complete personal history and family history for the presence of allergic manifestations was of utmost importance. We found, in our group, that 26 of the individuals gave a positive history of some form of allergy in the immediate family, such as asthma, hay fever, urticaria, and eczema. The individuals in 21 instances gave a history of other symptoms found to be definitely allergic or suggestive enough to be considered allergic. In analyzing these 21 cases, twelve gave a history of abdominal pain, nausea, vomiting, and abdominal distress after eating certain known foods. Another six had noticed nasal symptoms, while there were three who knew certain foods would cause them to have hives, two others asthma, and two some form of eczema, these women often giving a history of two or more symptoms. We believe that if a more careful history had been taken in the earlier cases, the incidence of allergic symptoms other than dysmenorrhea would have been higher.

In determining the sensitivity of the individual to foods and other substances, the common skin tests by the scratch method and by the intradermal reaction method were used. The substances other than foods for which tests were made were: pollens, house dust, silk, cotton, horse dander, insecticides, etc. In the cases giving a history of gastrointestinal symptoms, Rowe's trial diets were most helpful in eliminating the causative factors. The leucocytic reaction to sensitive substances probably would be of considerable value in studying cases of this type; however, it was not used in this series. The skin tests by both the scratch and intradermal methods were read in fifteen to thirty minutes. Quite frequently a more positive reaction was seen at the end of several hours. The most frequent reaction was of small elevated areas surrounding the test, with little or no erythema. We be-

abroad. On this account we feel that any patients who are suffering from essential dysmenorrhea should be thoroughly tested for causative factors before any such operation is performed.

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630 SOUTH KINGSHIGHWAY

THE FORGOTTEN MAN IN OBSTETRICS

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TOO often," said Robert B. Lloyd, "do we forget those who first forced their way along paths which in the future become well frequented thoroughfares . . . too often is the honor due to these pioneers pushed into the limbo of obscurity by the very weight and magnitude of the chain, the initial links of which they themselves had helped to forge."

It was so in the making of the obstetric science. There have been men whose names are seldom mentioned and whose works are little known, yet they forged the first links in the chain of observation and experimentation, and so were an essential part in the making of priceless contributions. They are the forgotten men in obstetrics.

The best robbed man in medical history was Soranus the Ephesian, who lived in the second century of the Christian Era. Throughout ancient and medieval times medical authors were not so meticulous as now in giving credit where credit was due. This, coupled with the singular incident that the books of Soranus "On the Diseases of Women" were unknown to succeeding generations until 1838 when August Lobeck of Königsberg translated them from the original Greek, accounts for the fact that for fifteen hundred years Soranus remained in comparative obscurity, his works garbled by all writers on obstetrics down to the time of Mauriceau at the end of the seventeenth century. It was Moschion, who probably lived in the sixth century, to whom much of the credit was given for the teachings of Soranus.

A disciple of Hippocrates, Soranus is now recalled as "The Obstetrician of Antiquity." Dissecting the human body he observed that "the uterus is not convoluted as in the brutes but more like a cupping glass," this in contradiction to the ancient writers who, failing to dissect the human body, assumed that the uterus of woman had two horns as in beasts. Verification of the observations of Soranus

Rowe's trial diets, No. 4 being found quite satisfactory. At the end of three months patient was free of pain, nausea and vomiting at menses. During the following two years, patient reported she was free of pain as long as she did not break her diet too often.

CASE 3.—E. J., aged nineteen years, student, single. Eczema of hands and arms for three years. Cramps for first two days of menses, severe first day. Brother has asthma. Physical and pelvic examinations negative, except uterus is tender to bimanual pressure. Menses, onset twelve years, every twenty-eight to thirty days, lasts four days. Onset of pain at beginning of menses. Skin tests positive to pork, eggs, milk, nuts, beans and chocolate, doubtful to beef, lamb, corn, wheat, and cream. Free from pain for four months while on diet, eliminating above foods. Eczema of hands and arms markedly improved.

CASE 4.—M. M., aged twenty-six years, married six years. One spontaneous miscarriage at three months three years ago. Menses, onset fifteen years, every twenty-eight to sixty days, lasts four to five days. Cramps with beginning of menses, severe for two days and sometimes throughout entire period. Mucous vaginal discharge for about two years, at times quite profuse. Has known for several years that eggs, bananas, tomatoes, and onions caused abdominal discomfort and nausea. Physical examination negative. Pelvic examination shows profuse thick white vaginal discharge, some in cervical canal. Cervix normal size, shape and position. No infection. Corpus normal size, shape, position, and mobility. Small ovarian cyst, left. Put on Rowe's diet No. 1, with relief of all pain. Diet increased to Rowe's No. 3. Next five successive menses, cramps were so slight that she did not want to do anything further. Encouraged to increase diet one food at a time.

CASE 5.—E. S., aged eighteen years, student nurse. Severe cramps, nausea and vomiting with menstruation. Irregularity of menstruation. Has known for many years that bread and pork would cause nausea and abdominal distress; if eaten excessively, vomiting and diarrhea. Onset of menses twelve years, every twenty-eight days to three months, lasts four days. Onset of dysmenorrhea and irregularity with onset of menstruation. Confined to bed one day always, frequently two days and occasionally cramps through entire four days. Physical examination and recto-abdominal examination were negative. Intradermal skin tests were positive to wheat, pork, chocolate, bananas, pepper, and house dust. On a diet free of the above foods, she immediately went free of all pain for four months. At this time diet was broken for two months of necessity, with return of dysmenorrhea and some irregularity. On two other occasions, for convenience, the diet was broken for one- or two-week intervals with partial return of symptoms. After being free of symptoms for seven months, graduated feeding of wheat, as is frequently done in allergic children, was started six months ago, beginning with a well-toasted cracker daily and increased to two slices of bread with each meal at the present time. The August and September, 1936, periods had a noticeable pain, which means that her tolerance has been exceeded and we must drop back to one slice or maybe two, well toasted. She has been under study for two years and ten months.

We are unable to suggest the frequency of allergy as a causative factor in the total number of those suffering from dysmenorrhea.

In conclusion we feel that this work shows very definitely that allergy plays part as a causative factor in essential dysmenorrhea. This is of particular importance since presacral sympathectomy has been rather frequently advocated in the recent past both in America and

We have referred to Ambroise Paré who is credited with having revived the ancient practice of podalic version, but Paré himself did not lay claim to such distinction. Called by Smellie "the famous restorer and improver of midwifery," Paré confessed that he had first seen the operation performed by Thierry de Hery and Nicole. While failing to popularize the procedure (this was the contribution of Mauriceau, Guillemeau and Portal), he extended the indications laid down by Soranus by resorting to version in severe hemorrhages and where immediate delivery was imperative.

Nearly a century before Carl Siegmund Credé published *Leitung der Nachgeburtsperiode*, in which he described his method of delivering the afterbirth by external manipulations, John Harvie, a modest and retiring associate of Smellie in the teaching of midwifery at Wardour Street, London, and the successor of the Lancashire Scot after he retired to his native village of Lanark, published an unpretentious book entitled *Practical directions showing a method of preserving the perineum in birth and delivering the placenta without violence* (London, 1776). While lacking in many of the details Harvie's work omitted none of the essential features which marked the technic of Credé, whose name is by common consent associated with the procedure. Harvie observed that if the placenta is delivered by nature alone or by gentle external manipulations, it will come away inverted. If delivered by force the reverse takes place; that is, the lobular side comes away first. Harvie's work appeared thirteen years before Baudelocque described the two ways in which the placenta extrudes from the uterus, and although about one hundred years had elapsed, the names of Schultze and Duncan were embodied in the two methods of placental protrusion.

There is much of romance in the history of ergot. Ranking among the great plagues of earlier times ergotism claimed 400,000 victims in France in 994 A.D., with sporadic recurrences of epidemics on the continent of Europe and in England until well into the nineteenth century. John Stearns (1770-1848) popularized the use of ergot in obstetric practice and defined its limitations, but ergot was administered as an oxytocic by Joachim Camerarius in 1588, and the midwives of France, Italy, and Germany are said to have employed the drug for generations. There is abundant evidence that throughout the Middle Ages midwives recognized the abortive qualities of ergot and prescribed it in their practice. Stearns tells of his attention having been called to ergot by an old woman who was an immigrant from Germany, and she probably acquired her knowledge of the drug in her native country.

Scipio Mercurio, a Dominican monk of Venice, Italy, in the sixteenth century, mixed his philosophy and theology with the study and practice of obstetrics. Possessed of all the eccentricities of a genius, this

came a thousand years later with Leonardo da Vinci (1452-1519) and Andreas Vesalius (1514-1564) in their graphic portrayals of the gravid uterus.

History records that Soranus was first to instruct midwives in the technic of podalic version, only to have this priceless invention all but discarded until the time of Paré early in the sixteenth century. He employed the knee-elbow position in the puerperium and delivered on the birth stool. While claiming no originality in either of these procedures, Soranus, and before him Hippocrates, anticipated the Trendelenburg position. To replace the prolapsed uterus they bound the knees, ankles, and hips to the rounds of a ladder and hoisted the ladder to the gables of the house. It was Soranus, not John Harvie in the eighteenth century, who first instructed midwives how to protect the perineum from injury in birth.

We are wont to think of gynecologic surgery as a modern invention, but there is abundant evidence that Soranus and his contemporaries performed major pelvic operations. Certain it is they who performed vaginal hysterectomies, probably by the application of the cautery. Commenting upon necrosis of the prolapsed uterus, Soranus said: "The blackened portion is to be resected in the same way as we resect the lobe of the liver or lung which has become necrotic from prolapse." When the Arabs took over the relics of Greco-Roman culture the operative art of the ancients gave way to the branding iron. Said Albucasis, greatest of Arabian surgeons: "The operative art has disappeared from among us almost without leaving any trace behind. Only in the writings of the ancients do we find some references to it, but these, by bad translations, by errors and alterations, have become nearly unintelligible and useless."

The birth figures of Soranus, depicting the fetus in utero in all manner of grotesque attitudes, were credited to Moschion of about the sixth century and garbled and distorted by Rösslin in the *Rosengarten*, published in 1520. They appeared in works on midwifery to the seventeenth century without acknowledgment of their original source. Ludicrous as they appear today, they were accepted in good faith until late in the fifteenth century when Leonardo da Vinci sketched the fetus within the uterus lying in its natural position.

Commentators tell us that Soranus was a diligent student of the works of past masters and faithfully acknowledged his obligations to them. It is unfortunate that posterity failed so signally in doing him the honor that was his due. He was above all others "the forgotten man in obstetrics." But he was not the only obstetrician pushed into "the limbo of obscurity," while credit was accorded to a successor more gifted in the art of publicity or more favored by social and professional contacts.

Eminent in the field of letters, Oliver Wendell Holmes is credited with having made one of the most signal pronouncements in the history of medicine. His essay on "The Contagiousness of Puerperal Fever," was indeed an inspired document, presented with cogent logic and withering satire. It was an assemblage of evidence gleaned from the literature and from personal correspondence but lacking the background of laboratory research and clinical observations which marked the contributions of Semmelweis. With no thought of disparaging the contributions of Holmes and Semmelweis, we recall that at the time Semmelweis was making his observations and experiments in the Vienna hospital, a young interne in the Maternité d'Paris was struggling with the same problem and ultimately arrived at almost identical conclusions. Later, he obtained results in the lowering of the maternal mortality of puerperal fever that were comparable to those obtained by Semmelweis. Stephane Tarnier knew nothing of the work of Semmelweis when pursuing his investigations, yet there was a striking similarity in their methods of procedure and in their results. It was he who introduced the term "puerperal septicemia."

Not until well into the eighteenth century was there anything approaching a clear conception of the contagious nature of the malady and even then it was not known that the disease could be conveyed from one individual to another. Living in comparative obscurity in the latter half of the eighteenth century Charles White "travelled along unknown paths which later became open thoroughfares." A contemporary of William Smellie and William Hunter, White stressed the retention of the lochia as an etiologic factor in puerperal fever and recommended elevation of the head of the bed to promote drainage; thus anticipating the so-called Fowler position. That he anticipated antisepsis long before the time of Lister is evidenced by the following quotation from his *Treatise on the Management of Pregnant and Lying-in Women* (London, 1772).

"I must not omit to mention in this place," said he, "the good effects I have experienced from emollient or antiseptic injections into the uterus, by means of a large ivory syringe, or an elastic vegetable bottle. . . . I have by this means known the fever much assuaged, and in many cases wholly extinguished." White stressed the importance of isolation of fever stricken patients and the disinfection of the lying-in wards; he advocated clean linens and the delivery of women in rooms set apart from the contaminated wards.

In the years 1790 to 1792 Alexander Gordon of Aberdeen was in the thick of an epidemic of puerperal fever. From clinical and postmortem observations Gordon arrived at the conclusions that the disease was contagious, that it was a specific disease affecting lying-in women. He pointed out that "the matter is readily and copiously admitted by the numerous patulous orifices which are open to imbibe it, by the separation of the placenta from the uterus."

monk of the Dominican order paid homage to no authority. To his mind Hippocrates was not infallible, Avicenna sometimes spoke nonsense, Aristotle was not always the wise philosopher and scientist, Averrois was fooled by the old wives' tale that women can become pregnant without a husband when in a bath, Galen was wrong in teaching that the uterus contains separate compartments and that early pregnancy can be diagnosed by the appearance of the urine, and the great Paré was remiss in failing to recognize the hymen.

Mercurio was the author of the first work on midwifery published in Italy. This remarkable work (*La Commare*, 1596) held a commanding position in Italy and Germany for 150 years. Two chapters are devoted to the subject of cesarean section in which the author was the first to suggest the cesarean operation in contracted pelvis. Writing of combined version, now credited to Braxton Hicks, Mercurio said: "The midwife ought to use her hands, whereby she keeps one hand in the birth canal and the other on the abdomen; she may try to turn the child's head downward and the feet upward. It may seem hard for the person who is not accustomed to manipulate but often it is easy to accomplish. One must not be in a hurry or excited, but wait patiently until the child is turned." He referred to the "hanging legs" position which Albucasis introduced in the tenth century, and Walcher popularized and was given title to in the nineteenth century.

Neither Braxton Hicks nor Marmaduke Burr Wright claimed priority in the technic of podalic version, save in the development of certain details in the procedure, each contending for the credit for having first suggested the part played by the external hand in facilitating the turning. That neither Hicks nor Wright is entitled to credit for originating the basic principles of combined external and internal version is clearly set forth in the records. Two and one-half centuries before the time of Braxton Hicks the Dominican monk (Scipio Mercurio) described a somewhat similar procedure in his "*Midwife*" book, and before him Hippocrates, Soranus and Rösslin referred to cephalic version by the cojoined action of the two hands. Wigand described the technic in detail in 1812 and Mme. La Chapelle (1769-1821) referred to cephalic version, only to condemn it.

Hendrik van Deventer of the Hague was first to call attention to the pelvic axis, but he is not entitled to the credit for priority in pointing out that the main cause of obstructed labor is to be found at the inlet of the pelvis. It was Mauquest de la Motte, a country practitioner in the village of Picardy, who is entitled to the distinction. Fashbender says, "History will record a prominent place for de la Motte in the doctrine of the narrow pelvis." This remarkable man made his daily rounds on horseback, and in his isolation he acquired a resourcefulness that marked him as an obstetrician of unusual attainments, perhaps the greatest of his time.

ANALGESIA IN LABOR CONSIDERED FROM THE STAND-POINTS OF MEDICINE AND PSYCHOLOGY*

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OBSTETRICS seems to be today at much the same turning point as a hundred and fifty years ago.

After 1730, the forceps, the "noble and beneficent" instrument of the Chamberlens, became generally accepted. It was used extensively by the French accoucheurs who were the leaders in obstetrics for more than a hundred years. They considered obstetrics as a branch of surgery and the art of delivery as a problem in operative skill. Smellie in England, on the other hand, resented the transformation of a natural process into an artificial one and placed obstetrics on an anatomicophysiologic basis. His work on the pelvis and Hunter's treatise on the anatomy of the pregnant uterus, laid down the fundamental principles of obstetric science; for, in obstetric thought, the size of the pelvis and uterine function are the poles around which all problems of labor revolve. To the present day the teachings of the English school, which rely more on the forces of nature than on the skill of man, dominate conservative obstetrics.

However, of late, the principles of the French school seem to have been revived. In the words of Plass¹: "The most striking change in obstetric practice in the last fifteen years has been the great increase in operative deliveries. A certain few have raised their voices against the tide of radicalism, but apparently without stemming its rise." The analysis given in the Fifteen States' Report² and the Report of the New York Academy of Medicine on Maternal Mortality,³ shows that there is at present too frequent and incompetent interference in labor. A marked increase in cesarean sections, in some hospitals as high as 500 to 1,200 per cent has taken place in recent years.⁴ Delivery by forceps, as a so-called prophylactic operation, is being recommended by some obstetricians as the safest method of terminating labor. To be sure, many accoucheurs deliver by forceps with a minimal risk; but the fact remains that operative delivery carries with it an added mortality and morbidity for mother and child.

I strongly share the opinion of many observers that a major cause of this disheartening situation is the increased use of analgesics in labor. This contention is borne out by a study of foreign statistics. In Holland and the Scandinavian countries, which have the lowest

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To Gordon should go the credit of recognizing puerperal fever as a wound contamination and for identifying the carriers of the contagion. Semmelweis believed the virus to be decomposed animal organic matter, which recalls the story that in the ninth century Rhazes, the Arabian, must have associated decomposed animal organic matter with disease. In order to determine the site of a hospital in Bagdad, it is said that he hung portions of meat about the city and where the meat was last to spoil, there he built the hospital.

Augustus Hauptman and Christean Langius had the misfortune to be born two hundred and fifty years too soon. Foreshadowing the observations of Schaudinn and Hoffmann they contended that the venereal poison was nothing other than "a numerous school of little nimble, brisk invisible living things, of a very prolific Nature, which when once admitted, increase, and multiply in Abundance; which lead frequent Colonies to different Parts of the Body; and inflame, erode, and ulcerate the Parts they fix on."

Their contemporary, John Astruc, physician to Louis XIV, retorted: "If it was once admitted, that the Venereal Disease could be produced by invisible living things swimming in the Blood, one might with equal Reason allege the same Thing, not only of the Plague . . . but also in the Small Pox, Hydrophobia, Itch, Fetters and other contagious Diseases . . . and thus the whole theory of medicine would fall down." Two hundred and fifty years later, says Howard Haggard, "Pasteur demonstrated that contagious diseases were caused by little living things, bacteria." In 1905 Schaudinn and Hoffmann found the organism of syphilis "swimming in the blood". . . and revealed their "very prolific Nature, which when once admitted, increase and multiply in Abundance; which lead frequent Colonies to different Parts of the Body (and inflame, erode and ulcerate the Parts they fix on)."

We are told that "He who cannot render an account to himself of at least three thousand years of time, will always grope in the darkness of inexperience and merely live from day to day." This is but another way of saying that the achievements of today are deeply rooted in the past.

Since normal uterine function is the all-important factor in the expulsion of the child, and since the character of the contractions is our best index of the progress of labor, the danger of any procedure which disturbs uterine function and distorts labor is obvious. In addition, uterine dysfunction predisposes to hemorrhage in the third stage. Furthermore, it is known that patients who are afraid before an operation often suffer from shock. This has been explained as damage to the cells of the higher nerve centers transmitted by afferent impulses from the trauma.¹⁰ Even deep surgical anesthesia is unable to overcome the influence of emotion. Hence, in labor, where fear is a major cause of pain, psychic damage cannot be prevented by anesthesia.

Finally, all analgesics cause a depression of the respiratory center of the fetus. Since inefficiency of this center is a striking characteristic of the newborn, the cause of such vague conditions as apnea, delayed respiration, asphyxia and atelectasis, when not due to gross birth injuries, is obvious in many cases.¹¹

Easy spontaneous delivery is of no little importance to the child, for it has been indicated by psychoanalysis that inability to overcome the birth trauma is one of the causes of neuroses in later life.¹²

In spite of what has been said here, many obstetricians claim that, without risking their practice, they are unable to resist the demand of women for short and painless labor. This shows a lack of proper education of the patient and a failure on the part of the physician to consider the important psychologic aspects of childbearing.

It is much to be regretted that so little work has yet been done on the psychology of pregnancy.¹³ Conception is often accompanied by a strong emotional reaction ranging from exultation in the case of successfully treated sterility to despair when the pregnancy involves social disapproval. Even in normal cases the pregnant woman is emotionally unstable and latent psychic disturbances often become manifest.¹³

Childbearing is so essential an experience to a woman that the thwarting of its normal course by the excessive use of analgesics may cause damage to her personality. If she is carried through delivery in an unconscious state, she is deprived of the experience of giving birth to her child, and in some cases she will pay for this escape from reality by nervous disorders.¹⁴

As shown by Read¹⁵ in his admirable book, *Natural Childbirth*, fear is the principal cause of pain in labor. The uterus is capable of producing rhythmic contractions independently of the autonomic and sympathetic nervous systems and, like other protected viscera, it has no nociceptors. Hence, uterine function should not be essentially painful. Observations of labor among primitive peoples bear out this conclusion.¹⁶

infant and maternal mortality, analgesics are used very judiciously, and operative delivery is resorted to only in about 3 per cent of the cases as compared to 20 per cent in New York.

It is not my intention to condemn analgesics altogether. I consider their use justified in the second stage of labor. However, I maintain that the routine administration of analgesics in the first stage is as wrong as any other indiscriminate medical procedure.

A study of the various drugs used shows that an analgesic which is perfectly safe for both mother and child has not yet been discovered.⁵ It seems that with the commonly used anesthetics, such as ether, chloroform, and nitrous oxide and oxygen, the mother carries the main risk. If applied intermittently during the second stage, their administration has been approved by all obstetric schools.

The drugs used to produce amnesia and analgesia, on the other hand, appear more dangerous to the fetus.⁶ Morphine and its derivatives, mostly used in combination with scopolamine, have been condemned by many investigators⁷ because they prolong the second stage and too often cause asphyxia in the fetus.

Gwathmey's analgesia, which is a combination of morphine with magnesium sulphate and rectal ether and quinine, is widely used.⁸ The following complications make it objectionable: rectal irritation, ether shock, arrested labor, fetal asphyxia and narcosis which are frequent and at times serious.

Recently the barbiturates have been introduced into obstetrics. Their pharmacologic action is hypnotic, sedative and antispasmodic, mildly analgesic and only in large toxic doses anesthetic. Judging from the clinical disadvantages mentioned by several investigators, large toxic doses have apparently been used. These disadvantages are⁷:

1. The administration requires the close attention of the physician or of two trained attendants, since in some cases restlessness and excitement result which make the patient difficult to control, especially during labor.
2. The initial drop in blood pressure and respiration after intravenous administration is sudden and sometimes alarming.
3. At times the analgesia is uncontrollable and must be counteracted by the prompt use of stimulants.
4. A decided increase in operative deliveries results and often deep apnea in the child.

All the drugs mentioned reduce uterine contractions, both in frequency and in strength, and thus interfere with normal uterine function.⁹ They prevent the very essential cooperation of the mother in the second stage, thereby causing an arrest of labor and making operative delivery inevitable.

The beginning of the second stage is marked by a change in the mental attitude of the patient. All feeling of futility is gone; she concentrates with deliberation on the task to be accomplished. In spite of the more painful contractions, resolution and courage take the place of resignation. We can now safely administer an anesthetic and thus make easier her full cooperation in the expulsion of the child.

The head should not be delivered at the height of a pain. At the proper moment, the mother is told that her baby is about to be born and asked to bear down slowly as the contraction subsides. The head is then delivered by preserving its flexion during its passage through the vulva, and with the onset of the next contraction the shoulders are lifted over the perineum.¹⁵ With proper management the vulva and the perineum are completely relaxed and permit the passage of the child without injury.

This active participation in giving birth to her child will be remembered by the mother long after the troubles of pregnancy and labor have been forgotten and will be cherished as an experience which she would not miss.

In the third stage the parental instinct appears with its overwhelming joy and tenderness to the baby enhanced by the pride of accomplishment. These emotions will be carried into the puerperium and further quick recovery.

In my observation no woman, whether intelligent or unintelligent, modern or old-fashioned, wants the birth of her baby to be a blank in her memory. Certainly, few will wish to be relieved of pain at the risk of harm to her baby.

It is to be hoped that future chemical and pharmacologic work will provide us with more satisfactory analgesics. Research on the psychology of childbearing, too long neglected, should be even more valuable, for, as here indicated, new drugs are needed less than improved obstetric management.

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Religion and folklore, as well as early obstetric practices, have produced in civilized woman a fear of childbirth which, if not overcome by proper psychologic management, constitutes a serious obstacle to normal parturition. Much damage is done by irresponsible allusions to the dangers of childbirth and by sensational magazine articles which have gone so far as to advocate cesarean section as the only humane method of delivery.

The discomfort at labor is not intolerable. Labor pain is intermittent, lasts only a limited time and is followed by a natural amnesia. Its function sets it apart from pathologic pain, a fact which is readily understood by the patient and deserves greater recognition by the physician. If the question of pain relief is raised by the patient, which by no means happens in every case, we assure her that she will be given all the relief necessary for her and compatible with the safety of her child, thus indirectly conveying the idea that drugs are not always harmless to the baby.

If childbirth is such a profound experience in a woman's life, it is the duty of the obstetrician to make it a happy one and not an ordeal or a tragedy. The physician should realize that he has an important function as an educator. The obstetrician is fortunate in having nine months in which to teach the patient sound ideas about childbearing. Much can be accomplished by giving her a good book to read, and careful psychologic observation should be made a part of the prenatal care. With sufficient psychologic ability, the physician should be able to win her absolute confidence and thereby dispel all doubt and fear.

To be sure, there appears during the last weeks of pregnancy an irrational awareness of the mystery to be experienced by each woman for herself at the time of delivery, but it would be a mistake to interpret this inarticulate sentiment as fear of pain.

The keynote of the successful management of labor is the conscious participation and cooperation of the patient. She should observe her contractions and keep a record of them while they are still mild. If taught that hard, long contractions are the ones which will accomplish the birth of her child, she will wait eagerly for the "good" contractions and discount the occasional light ones.

During the tedious first stage of labor, the psychologic skill of the physician is all-important. He should attempt to preserve as long as possible the elation which the patient experiences in anticipating the coming of her baby. Later, he should guard against fear and exhaustion by his cheerful confidence and assurance that all is well and by encouraging relaxation. If necessary, he may administer a single small dose of analgesia for the purpose of dulling the activity of the mind rather than producing insensibility to pain or even unconsciousness.

CHROMIC ACID FOR THE TREATMENT OF CHRONIC INFECTIVE ENDOCERVICITIS

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DURING the past twenty years, I have treated 250 cases of chronic infective endocervicitis by the use of chromic acid with its complete eradication within a short time, five to seven weeks. After a follow-up period of from five to fifteen years during which neither cervical stenosis nor interference with labor has been encountered, the restraint for designating this method of treatment successful is completely removed.

It is to be remembered that the seat of this pathology is in the endocervical glands, which are imbedded in the fibromuscular coat, and exposed to irritation and congestion with the elaboration of a profuse exudate. This leucorrhea by its alkalinity reduces the hydrogen ion concentration of the vaginal secretion with resultant cervical erosion. If one remembers also that occlusion of the gland ducts by fibrous tissue results in cyst formation (ovula nabothi), the clinical picture of chronic infective endocervicitis is again vividly portrayed.

The fact that chromic acid as such is antagonistic to the alkaline cervical leucorrhea and in addition to coagulating, possesses an oxidizing property which increases its penetrating power, suggested the feasibility of its use as an effective agent for treating chronic cervical leucorrhea.

METHOD

Requirements.—Chromic acid (crystals or liquefied), alcohol, hydrogen peroxide or caroid solution, alcohol lamp, long metal applicator flattened or threaded at the tip, vaginal bivalve speculum, uterine sound, pledgets of cotton, and rarely a cervical tenaculum.

Preparation.—The patient is placed in the lithotomy position, vaginal speculum inserted, vagina cleansed, exudate removed from cervical canal with hydrogen peroxide or caroid solution on pledgets of cotton, direction and depth of cervical canal ascertained with uterine sound, a pledget of cotton saturated with alcohol is placed under the posterior cervical lip in the speculum for protection from any chromic acid excess or overflow during its application.

Technic.—Chromic acid (4 to 6 granules) fused on the flat end of the applicator over the alcohol lamp or the liquefied acid on a small pledget of cotton wrapped on the threaded end of the applicator, is introduced into the cervical canal one-fourth its length for thirty seconds. The applicator is rotated so that the acid comes in contact with the entire circumference of the canal. No anesthetic is required. After its withdrawal, the patient remains on her back for three minutes to insure retention of the acid within the endocervix.

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OSLER BUILDING

McEuen, Selye and Collip: Some Effects of Prolonged Administration of Oestrin in Rats, Lancet 1: 775, 1936.

The authors report the results of subcutaneous injections into castrate female rats of estrone for periods longer than 132 days. Simple enlargement of the pituitary occurred in 8 of 12 rats. These changes were less marked in castrates. Six castrate females, initially three or four months old, received daily subcutaneous injections of 20 γ of estrone (in corn oil) for 331 days; vaginal estrus was maintained with few lapses. Then for another thirty-day period all estrone was stopped in five, but some of these were given crystalline progesterone. In all five an anestrus state returned and when sacrificed no material differences were discovered. The findings were: hypertrophic fibrosis, squamous metaplasia, enlarged pituitaries, multiple mammary milk cysts, enlarged adrenals. The sixth rat, which received estrone the full period, had atrophy of the adrenal cortex.

Due to the source of these rats hereditary tendencies toward tumors were removed.

H. CLOSE HESSELTINE.

Electrocauterization, Dickinson,⁴ requires expensive electrical apparatus and technical skill and essentially reduces rather than eradicates the infection by the technic (linear cauterization) generally advocated; and complications following cauterization of the cervix uteri have been reported, Cannell and Douglass.⁵ Electrocoagulation, Ende,⁶ in addition to being more expensive than electrocauterization, is more technical; but has the advantages of neither carbonizing the tissues nor ultimately producing scar tissue, since its healing process is anaerobic. However, death following coagulation of the cervix has been observed, Hiller.⁷ Furthermore, an elongated cervix would be treated effectively with great difficulty with the usual cervical coagulation electrode.

Conization, Hyams,⁸ not unlike the surgical method both in the skill required and results obtained, obviously is best reserved for the postnubile period.

It seems, therefore, that any method employed for the treatment of chronic infective endocervicitis nonsurgical, inexpensive, practical, a home or office procedure, requiring no technical skill, easily controllable, not contraindicated by childbearing, void of serious complication or sequela, giving from 99 per cent to 100 per cent satisfaction within a reasonably short time and with the patient always ambulant, is deserving of more than casual consideration. Such is the record in my experience from the use of chromic acid.

The writer therefore commends its use to the profession as a safe, sound, and satisfactory method of treatment, not alone for the excellent results obtained, but as a possible stimulus to further investigation with a view of discovering or developing, perhaps, a better or more desirable method for the eradication of this perennial, embarrassing, and heretofore unsatisfactorily treated condition which comprises such a large percentage of current gynecologic pathology.

SUMMARY

1. The successful treatment of 250 cases of chronic infective endocervicitis by the use of chromic acid is discussed.
2. No worth-while consideration, complication or sequela contraindicates its employment except acute adnexitis.
3. The method is nonsurgical, inexpensive, a home or office procedure, and requires no anesthesia or technical skill.
4. A critical discussion of the prevalent methods is presented.
5. Use of chromic acid for the treatment of chronic infective endocervicitis is commended to the profession.

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Similar applications at seven-day intervals are repeated, including an additional one-fourth length of the cervical canal each time, the last extending to the internal os. Four applications are thus required to complete the treatment.

The chemical action of the chromic acid could be readily controlled by the application of alcohol to the treated area; but since penetration is the primary requisite for reaching and eradicating the deep-seated pathology, such use of alcohol is never required.

The accompanying cervical erosion obviously requires no special treatment, as it heals following each endocervical application of chromic acid in direct proportion as the reaction of the vaginal secretion returns to normal (acid). However, touching the eroded area with the chromic acid facilitates its healing.

Complicating nabothian cysts are adequately treated by puncturing with a bistoury, evacuating their contents, and touching their cavities with chromic acid on the applicator.

The patient should be advised of the following by-effects of the treatment: The alcohol on the cotton may cause a stinging pain in the vagina for a short time; the leucorrhea increases in amount one to three days following each application; an offensive odor from the discharge requiring the use of a deodorant appears after the second or third application; rarely, about one hour following the fourth application, there may occur abdominal pain, nausea and vomiting due to entrance into the uterine cavity of a small amount of the chromic acid. These soon pass off and require no treatment; menstruation may be slightly prolonged should it occur during the treatment interval.

One week after the last application the patient is instructed to take a cleansing vaginal douche of lysol or creolin (1 per cent once daily for two weeks, douches previously not having been allowed. She may notice the eschar or necrotic plug washed from the endocervix during a douche.

The patient is instructed to return for final examination at the end of the douche period when one will find that the leucorrhea has ceased, the erosion healed and the cysts of Naboth have disappeared; previous hyperplastic and/or everted cervical lips are normal; the treated surface is smooth and epithelialized; and the external os again presents the operculum. The only contraindication to the use of this method worthy of consideration is acute adnexitis.

The nonsurgical methods heretofore employed for the treatment of chronic infective endocervicitis are legion and have included practically anything from a simple vaginal douche of table salt and baking soda to the endocervical application of radium, including tamponade, intra-cervical medicinal injections, ionization, galvanism, suction treatments, etc. But owing to the unique anatomical pattern of the cervix uteri, the location and peculiarity of the involved pathology, and the extreme difficulty in reaching the seat of the trouble, the results of those methods have been generally disappointing to both the patient and the physician.

The merits and shortcomings of a few of the prevailing methods in use including surgery may be briefly discussed:

The surgical methods of Schroeder,¹ Sturmdorf,² Simon,³ might be summarized with the comment that although efficient, they are contraindicated during the child-bearing period in which the endocervicitis is most prevalent, because of the resulting scar tissue which would offer a serious complication in labor. It is also strictly a hospital procedure requiring anesthesia and surgical skill.

nities offered for discussion and the interchange of ideas at an occasion of this kind are not to be denied even if the gathering were to involve only a single or a limited group of nations. And so the United States might well take steps to hold a national congress within its own boundaries in the near future, say in 1939.

The fact might be revealed that preliminary discussion has taken place in various national and district society groups and the consensus of opinion has been the advisability of turning over the preliminary arrangements at least, to the American Committee on Maternal Welfare, the membership of which includes representatives from all the interested and important national and sectional groups. As a matter of record, resolutions of endorsement have been approved by various groups, including the American Gynecological Society, the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, the Central Association of Obstetricians and Gynecologists, and the Section on Obstetrics and Gynecology of the American Medical Association.

If a National Congress can be assembled it must be comprehensive in all respects, especially in the sense that it should include not only the specialist but the general practitioner; likewise the social service worker, health officer, and nurse should be invited to participate in its deliberations. This gathering must not be just "another medical meeting," it must have a wider appeal. The program should be based primarily on the presentation and discussion of topics and problems that are still unsolved as well as those about which we have accumulated but not always correlated knowledge. The contemplated congress must be held at a centrally located city with adequate facilities for its varied purposes, preferably in the month of June or September. The call should be nation wide, so as to reach every practitioner of medicine who is interested in this branch, as well as all public health authorities because of their close connection with maternal welfare work, and finally, the many lay organizations which have contributed so much to the preparations for better maternity care.

This announcement of a contemplated national congress might act as a challenge to the members of the American medical profession and in this way draw from them suggestions and comments. For to be successful, the Congress must be in response to a demand, it must reflect a desire for information and discussion, it must impress itself on the public as well as the professional mind, as a means to an end.

The JOURNAL is desirous of giving its support to the contemplated movement and in subsequent issues will present to its readers further information as this develops.

In the meanwhile it is hoped that those to whom the preliminary steps have been entrusted will, at an early date, proceed to outline the scope and purposes of a national gathering of those concerned with and interested in this important branch of medical practice.

American Journal of Obstetrics and Gynecology

EDITORS: GEORGE W. KOSMAK, M.D., AND HUGO EHRENFEST, M.D.

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Editorial Comment

A National Congress of Obstetrics and Gynecology

INTEREST in the welfare of womankind is age old. Within historic times, however, it has been based largely on sentiment, religion and conventional standards of morality, rather than on knowledge and reason. And as for the care of women during pregnancy or the multitudinous complaints originating from or ascribed to her generative organs, it is scarcely a hundred years since obstetrics and gynecology as a distinct branch of medicine began to grow and develop into the recognized specialty of the present day. A vast amount of knowledge has accumulated and many physicians have taken up the study and practice of obstetrics and gynecology as their life work. Clinics, research laboratories, and hospitals in great number have been dedicated to this specialty and meetings of those immediately interested in the subject are held during each year at different places and at varying intervals for the discussion of scientific and practical problems. Obstetrics and gynecology, particularly the former, have developed a much wider sphere of interest than that limited to their practitioners; there are important public welfare aspects to be considered as well as the wider fields of general medicine and surgery and the somewhat narrower ones of eugenics, sociology, etc. The progress, even the survival of the human race are questions to be considered by the student of maternity.

Problems naturally develop with the expansion of knowledge, problems which can be demonstrated and discussed most successfully at a meeting of minds and persons. Congresses, both international and national, afford such a means. The last International Congress of Obstetrics and Gynecology was held in Berlin in 1912. Efforts since the Great War to develop another have not met with much success. The uncertainties of European politics, the universal depression, the lack of an impelling force, have made very difficult an international gathering. Holland, however, is attempting to do so and has called a Congress to meet in Amsterdam in 1938. How much support it will receive from other countries naturally is uncertain in view of the disturbed conditions in Europe and elsewhere. However, the opportu-

advance in age of the mothers and especially in those who had had a number of children. Most of the large children were born in June and the least number in April. More of the children were males. Other causal factors seemed to be heredity, constitution and frame of the parents, and prolongation of pregnancy. Labor is usually easier than expected except in primiparas. Difficulty is encountered only because of the large size of the baby and not because of malpresentation or uterine inertia. Most of the complications consist of atonic hemorrhage, perineal lacerations and premature rupture of the membranes. Spontaneous delivery occurred in 73 per cent of the cases. The maternal mortality was 1.3 per cent and the fetal death rate was very high. (The author does not give the fetal mortality.)

J. P. GREENHILL.

Pape, Walter: Excessively Large Newborn Babies, *Ztschr. f. Geburtsh. u. Gynäk.* 105: 370, 1933.

In Osnabrueck (Westphalia) 558 of 4,165 (13.4 per cent) newborn babies weighed over 4,000 gm., an unusually high percentage in comparison with reports from Berlin, Dresden, and Munich (3 to 4 per cent); height and weight averages of the parents were above the normal. Many mothers were found habitually to give birth to oversized babies. Mothers very often made the statement that they themselves had been excessive in weight at birth. Many factors, such as diet, rapid weight increase of the mother, seasons, weather, early or retarded menarche, regarded responsible for oversized babies were found to be of no significance. An unusually large number of primiparas are among the mothers. The duration of pregnancy was found to have a distinct bearing upon the baby's size. Many of the patients went beyond term. The mothers were generally tall and strong, a characteristic of the Westphalian stock. No contracted pelvis was encountered. Of the deliveries 96 per cent were in cephalic presentation, 2.3 per cent in breech. The mechanism of labor resembled that of the contracted pelvis. The fetal heads were unusually hard and unyielding. Uterine inertia, long second stage of labor, operative interference, atonic postpartum bleeding occurred more often than with the normal-sized baby. Ten mothers died, 4 from sepsis, and 3 from peritonitis. The author concludes that the prognosis for both mother and child is less good than in those with normal-sized babies. The importance of early diagnosis of oversize of the fetus is stressed, but without stating how this can be done with any degree of certainty. Nevertheless certain points in the history of the patient bear weight, such as previous delivery of a large baby and the frequent occurrence of excessively sized babies in certain families. Cases that are diagnosed should be terminated before term or at least at term.

GROVER LIESE.

Kimura, Y.: Japanese Statistics on Large Newborn Infants, *Jap. J. M. Sc. Gynec.* 1: 61, 1936.

Among 24,058 full-term labors in the Tokyo Royal University Clinic there were born 190 infants weighing more than 4,000 gm. Of these, 175 weighed between 4,000 and 4,500 gm., only 12 between 4,500 and 5,000 gm., and but 3 above 5,000 gm., the largest being 5,150 gm. Not rarely the same mother has two or three infants of excessive size. Usually the mothers are well built; there was only one instance of true pelvic contraction among them. Multiparas amounted to over 92 per cent. In many cases the duration of pregnancy seems abnormally long, the average being 289 days, but in almost 19 per cent more than 300 days. The ratio of male to female infants was 141 to 100. Complications of pregnancy were comparatively rare, 10 in the 190 women. In contrast stand the complications of labor. For primiparas the average of labor amounted to over twenty-seven hours, for multiparas approximately

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

THE NEWBORN INFANT

Uchimura, Kenji: Group Specificity of Amniotic Fluid and Its Relation to Blood Group of Newborn and Mother, *Tohoku J. Exper. Med.* 28: 260, 1936.

Uchimura investigated this problem in 130 cases and found that fresh or concentrated amniotic fluid contains no isoagglutinins. With absorption of agglutinin the fluid shows the Types O, A, B and AB exactly like blood. The relations of group types between maternal or fetal blood and amniotic fluid are as follows: In about one-third of the cases fetal and maternal bloods belong to the same group; in the other two-thirds they are different. In this latter larger group he found the largest percentage (almost 60 per cent) of instances in which the amniotic fluid and newborn's blood belonged to the same group, the fewest cases (8.5 per cent) in which the amniotic fluid belonged in the same group with the mother's blood.

The article brings a detailed description of the technic employed in these studies.

HUGO EHRENFEST.

Uchimura, Kenji: Blood Groups of Newborn and the Paradox Phenomenon, *Tohoku J. Exper. Med.* 28: 272, 1936.

Investigating the cord blood immediately after expulsion of the child, the writer ascertained that in 130 cases the blood of the mature child in general shows the same percentual distribution among the various groups as the blood of adults. In the majority of instances (76.6 per cent) the isohemagglutinin originates in the child, in only 7.2 per cent in the mother. Only in a few cases there is a discrepancy with the blood type rule and the fetal agglutinin is identical with that of the mother. In these cases the agglutinin titre of the fetus is markedly low. This paradoxical phenomenon cannot be ascribed to the fact that in the newborn's blood the agglutination titre of the plasma usually is lower than that of the serum. It can be assumed that the circulating blood does not contain agglutinin but that this characteristic faculty develops only after the blood has been taken out of circulation. These findings contradict the assumption of Hess that agglutinins in large quantities pass from the mother during pregnancy into the fetal circulation or particularly in the moment of separation of the placenta.

HUGO EHRENFEST.

Nakagama, J.: Research on Gigantic Children, *Jap. J. Obst. & Gynec.* 15: 504. 1932.

Among 14,027 deliveries at the Kyoto Imperial University there were 153 children (1.09 per cent) who weighed over 4,000 gm. and 10 newborn (0.07 per cent) who weighed more than 4,500 gm. These large babies increased in number with

result of pressure of the latter into crevices running from the surface of the leaflet into the stroma. This latter view is supported by wax model reconstructions and by analysis of demonstrable facts. There is no pathologic significance to these nodules; they are a common anatomic finding. They have been found most commonly between the seventh month of intrauterine and the fifth month of extrauterine life.

W. B. SERBIN.

Stohr, G.: Malformations of the Heart of the New-Born, Arch. Path. 17: 311, 1934.

Two cases of congenital malformation of the heart are described, both cases having similar lesions apparently produced by factors operating in the same way. In both cases the abnormalities were confined to the heart only, thus pointing to an etiologic factor acting locally. A hereditary etiologic factor was excluded by a careful familial history. The author then proceeds to corroborate the theory of inflammatory genesis of the lesions. Both macroscopic and microscopic evidence are presented.

In both cases the gross malformation was evident chiefly on the left side of the heart; there was involvement of the proximal portion of the aorta, but the interventricular septum was completely developed. The combined lesions of malformation and endocarditis of the left ventricle (according to Rauchfuss) point to a postnatal type of primary endocarditis, since in cases of developmental deformities of the heart with secondary endocarditis, the inflammatory lesion is usually in the right side of the heart. The absence of a septal defect in both cases indicates that the development of the abnormality must be assigned to a period later than the seventh or eighth week of intrauterine life, because the septum normally is closed by this time. In both cases there was an almost identical thickening of the endocardium, projecting into the myocardium, with extensive formation of elastic connective tissue. This picture corresponds to the phase of healing in a postnatal inflammatory condition, and indicates a reparative process. The extensive development of new capillaries and capillary leucocytosis are usual concomitants or sequelae of inflammation. In both cases the most extensive lesions were found within the capillary muscles, where necroses and calcifications indicate the past influence of toxic processes.

W. B. SERBIN.

Plaut, A., and Sharnoff, G.: Acute Valvular Endocarditis in the New-Born, Arch. Path. 20: 582, 1935.

These authors report a case of acute mitral valvular endocarditis in the newborn with a review of the literature. The case occurred in a six and a half months' fetus; the mother gave a history of having had influenza three weeks prior to delivery. The birth was premature and the baby lived one and a half hours. Serial sections of a valvular hematoma on the mitral valve were made. Microscopic examination of these sections revealed a fresh thrombus attached to the leaflet at a point definitely separated from the hematoma. This vegetation consisted of a fibrinous network diffusely permeated by polymorphonuclear leucocytes and different cells with medium-sized nuclei; some of these stained deeply with hematoxylin. The endothelial lining of the leaflet was missing at the point of attachment of the vegetation; no bacteria could be found in the sections; the myocardium was normal.

A causal relationship between the previous attack of the mother's influenza and the fetal endocarditis seems improbable, nor was there any relationship between the hematoma and the vegetations, because there was normal intervening tissue between these two lesions. Such cases are extremely rare.

W. B. SERBIN.

nine and one-half hours. About 39 per cent represented pathologic labors; most common were atonic hemorrhages, secondary inertia and maternal injuries. Almost 20 per cent required operative interference. Striking was the prevalence of breech presentations, 5.8 per cent. Only two mothers died, one from a uterine rupture, the other from a premature placental detachment. The fetal mortality was high, 10 per cent (usual mortality in the clinic being 2 per cent).

HUGO EHRENFEST.

Gaujoux and Blanchard: Recurrence of Fetal Malformation, *Bull. Soc. d'obst. et de gynéc.* 23: 563, 1934.

Recurrence of fetal monstrosities is rare. In the Strassburg Clinic among 17,000 labor cases there were 40 monstrosities but only two of these were recurrences. The authors recently observed a case in which the first child had a hydrocephalus while the second child had an anencephalus. Wassermann tests were negative. Halbrecht believes such cases are due to hereditary syphilis in the second and third generation and advocates early and intensive specific treatment for the mother of a malformed infant.

J. P. GREENHILL.

Goldmaier, E.: The Inheritance of Monstrosities, *Monatschr. f. Geburtsh. u. Gynäk.* 99: 2, 1935.

In the Frankfurt Clinic during the last ten years among 13,920 labor cases, there were 36 cases of monstrosities among the newborn. Goldmaier investigated the heredity of these monstrosities. Only 22 cases could be properly studied and among these the author found a definite hereditary factor in 9. He discovered that heredity did not manifest itself in exactly the same form every time and that there were nonspecific tendencies toward monstrosities.

J. P. GREENHILL.

Diamond, M.: Calcification of the Myocardium in a Premature Infant, *Arch. Path.* 14: 137, 1932.

Diamond reports a case of calcification of the myocardium in a premature infant who lived for thirty minutes. The pathologic changes in the heart muscle were secondary to toxic degeneration of the muscle fibers. Inasmuch as no evidences of infection could be found in the fetus, it was assumed that the toxic agent originated in the mother. Fatty degeneration plays no part in calcification of the muscle fibers.

W. B. SERBIN.

Levinson and Learner: Blood Cysts on the Heart Valves of New-Born Infants, *Arch. Path.* 14: 810, 1932.

Levinson and Learner describe elevated dark red nodules found on the leaflets of the heart valves of the newborn as small cysts filled with blood. They occur on the mitral and tricuspid valves with about equal frequency; less often on the pulmonic and rarely on the aortic leaflets. In their series the incidence is 75 per cent; they are rarer after the first six months and very rare after two years.

Histologically, these nodules appear as monolocular or even multilocular spaces filled with red blood cells; the partitions between the spaces were not complete, thus indicating a communication between the compartments. The spaces are lined by a single layer of endothelial cells, similar to the surface epithelium of valve leaflets. There are 4 possible explanations for these nodules, viz.: (1) hematomas, (2) ectatic or dilated blood vessels, (3) angiomas, (4) spaces filled with blood as a

Smellie, J. M.: *Intranatal and Neonatal Death*, Lancet 2: 1453, 1935.

This study is based on the records of 99 infants whose deaths had been reported to the coroner for the city of Birmingham. All of these died suddenly or unexpectedly within the intranatal or neonatal period.

The deaths were classified as stillborn, 21; asphyxia neonatorum, 37; intracranial hemorrhage, 17; and bronchopneumonia, 11; while congenital defects, supranatal hemorrhage, volvulus, septicemia and violent death totaled only 13. In this series 75 failed to survive because of factors directly attributable to birth, 15 died from disease not directly associated with birth factors, 4 died from congenital anomalies, while 5 died from violence.

These constitute a highly selected group and form but a small number of the total stillbirth and neonatal deaths in the city during the same period. The group studied represent a valuable collection because these deaths occurred in a section of the population outside institutional guidance or control and with very little medical supervision.

H. CLOSE HESSELTINE.

Sellers, T. B., and Sanders, J. T.: *Analysis of 151 Consecutive Fetal and Neonatal Deaths*, South. M. J. 28: 1017, 1935.

The authors analyze 151 fetal and neonatal deaths occurring in a general private hospital in a series of 3,023 deliveries handled by about 100 different physicians. Excluding the deaths of 22 macerated and 21 nonviable premature infants there remains a mortality percentage of 3.6. Intracranial injury was present in 38 of the 63 deaths among term infants. Though 13 deaths of term infants are listed as due to asphyxia and atelectasis, the authors believe that many of these may have been due to undiagnosed intracranial injuries. A variety of causes of death are given for the 45 viable premature babies. There were almost twice as many deaths following operative as following normal deliveries. The authors found intracranial injuries in 11 infants of 14 delivered with high forceps. They believe that the fetal mortality in a general hospital can be reduced greatly by early consultation resulting in early diagnosis of abnormal conditions, and the timely application of proper surgical measures; that the high fetal mortality accompanying the use of forceps can be reduced by judicious substitution of cesarean section; that fetal mortality can be reduced by causing every accoucheur to possess accurate knowledge of the newer methods of resuscitation, avoiding such violent methods as swinging, contrast baths, and forced mouth-to-mouth insufflation, and having proper equipment for resuscitation in every hospital handling maternity cases.

EUGENE S. AUER.

Nattrash, Roland H.: *Prevention of Intracranial Injuries of the Newborn*, Brit. M. J. 2: 766, 1934.

The author reports 107 necropsies, 46 per cent of which showed the presence of intracranial injuries.

In discussing the mechanical causes of injury the author states that injury results when stretching of the supportive apparatus of the head, particularly of the tentorium cerebelli, is excessive. This occurs in cases of excessive molding and when the change in shape of the fetal skull is accomplished too quickly in an operative delivery. Exaggerated molding may be prevented by anticipating cephalopelvic disproportion and performing premature induction of labor or, if necessary, cesarean section at term.

The author further states that breech delivery is ten times more likely to give rise to cerebral injuries than vertex deliveries and warns against drawing the un-

Chase, W. H.: Infections in the New-Born, *Canad. M. A. J.* 32: 2, 1935.

In a series of 445 consecutive autopsies upon babies under one month of age, 119, or 26 per cent, presented gross or microscopic evidence of infection. Pneumonia was found in 97 (81 per cent). A classification based on the probable primary focus was used:

1. Metastatic infections: (a) Intrauterine 9 and (b) extrauterine 8.
2. Aspiration infections, intra- or extrauterine: (a) Products of conception 17 and (b) food or nasopharyngeal material 21.
3. Bronchial or peribronchial infections, without discoverable extrapulmonary focus; extrauterine 42.

In the absence of specific spirochetes in the tissue, a diffuse interstitial proliferative reaction in many parenchymatous organs was accepted as evidence of congenital syphilis. Aspiration was the immediate cause of death in most cases of congenital syphilis.

The aspiration pneumonias had clinical and pathologic characteristics which differentiate them from other bronchial and peribronchial infections.

Otitis media was the most commonly associated suppurative lesion and was confined almost entirely to the extrauterine respiratory infections.

Although the clinical picture was nonspecific and indefinite, a definite anatomic classification of pneumonia has been found applicable.

H. CLOSE HESSELTINE.

Carter, H., and Osborn, H. A.: Neo-Natal Dermatitis, *Brit. M. J.* 1: 465, 1936.

Pemphigus neonatorum is a subepithelial infection starting as a localized blister and spreading by contact infection. It differs from impetigo bullosa of older infants in that the latter is an intraepithelial dermatitis. Pemphigus is caused by staphylococcus aureus in the majority of cases. Silver nitrate (20 per cent) injected into the original blister prevents extension of the disease. For prophylaxis all attendants with skin lesions should be barred from the maternity and nursery units.

In Mill Road Infirmary where pemphigus was endemic for many years no cases occurred after methods of laundry and disinfection of clothing were revised and the laundry staff put under the direct supervision of the medical staff.

F. L. ADAIR AND E. L. POTTER.

Meltzer, Sara: Meconium Ileus, *Canad. M. A. J.* 34: 186, 1936.

This baby was the third child. The first child died on the fourth day from bowel obstruction. The second child is living. This baby began to vomit shortly after birth. On the second day of life intestinal obstruction was diagnosed and a laparotomy performed. There was meconium in the peritoneal cavity but the rupture was not investigated, only drainage was instituted. Death occurred forty-eight hours after birth.

At autopsy there was no evidence of peritonitis. The bowel was greatly distended, increasing gradually from the duodenum to the ascending colon. The distention stopped suddenly at the splenic flexure. Below this level the bowel was apparently normal. A rupture was found at the hepatic flexure. No bands or adhesions were discovered. A meconium plug was blocked at the splenic flexure, while none was below this level. The meconium was yellowish, thick and extremely tenacious.

After reviewing the literature, the author suspects that this baby had an occlusion of the pancreatic duct, a point overlooked at the autopsy. The first child died apparently from a congenital gastrointestinal anomaly also.

H. CLOSE HESSELTINE.

encephalitis. The history of the labor and its effect on the newborn may be of value in arriving at a diagnosis. The temperature, spinal fluid findings and leucocyte count depend upon the severity of the superimposed infection.

The macroscopic appearance of the brain may be normal if the injuries were slight, or may be altered by recent infection. In severe cases, small yellow nodules, grayish white plaques or the formation of minute cysts may be seen, and the brain may be focally or diffusely firm, with shrunken gyri, most commonly of the frontal and occipital lobes. The most extensive lesions are hemorrhages, porencephaly, atrophy of the entire hemispheres or sclerosis of the hemispheres. The meninges may or may not be thickened; the falx cerebri and the tentorium cerebelli may show evidences of old rents or hemorrhages. Microscopically, there may be presclerotic or sclerotic foci, with colloid deposits, or formation of cysts. These latter are suggestive of trauma sustained at birth. The prognosis, however, is not necessarily fatal.

W. B. SERBIN.

Sjovall, A.: *Cephalhematoma of the Newborn*, Acta obst. et gynec. Scandinav. 15: 443, 1936.

A review of 171 cases of cephalhematoma of the newborn is presented. Since these occurred among 40,252 newborn babies, its incidence was 0.4 per cent. In 80 cases, the cephalhematoma was discovered during the first week after delivery, in 40 cases it was noticed during the first two days and in 10 instances on the day of birth. In 50 per cent of the cases the hematoma was over the right parietal bone. In 20 per cent of the cases a major obstetric operation may have been responsible for the hematoma. In more than 70 per cent of the cases the mothers were primiparas and their labors were longer than usual. Three-fifths of the babies were males; hence a constitutional factor may be of importance in the development of cephalhematomas.

J. P. GREENHILL.

Birke, L.: *Birth Injuries of the Nose*, Monatschr. f. Geburtsh. u. Gynäk. 98: 144, 1934.

The author investigated a series of 542 newborn babies within the first eight days of life. In only 23 of all these cases did he fail to find some differences between both halves of the nose. In all the rest, definite differences were noticeable. However, in only 9 cases could these differences be associated with the course of labor. Injuries to the bony portion of the nose were observed in 3 cases. Among the 9 cases of possible birth injury to the nose there were 4 complicated cases of labor.

J. P. GREENHILL.

Moncrieff, Alan: *Nasal Obstruction in the Newborn*, Brit. M. J. 1: 1295, 1936.

Breathing takes place exclusively through the nose in the newborn period, even though the mouth may appear to be open. The ability to breathe through the mouth develops by about the tenth to the fourteenth day of life. When nasal obstruction is present in the early days of life, it may prove fatal. That the newborn may have great difficulty in acquiring mouth breathing is demonstrated by the histories of several cases. The obstruction may be bony and permanent or inflammatory and temporary.

The author emphasizes the importance of investigating the nasal airways in any newborn infant who has apparent difficulty in breathing. A soft rubber catheter, lubricated, may easily be passed through each nostril. If obstruction is present, an airway must be maintained through the mouth for about ten days, until the baby

molded fetal head too violently through the pelvis. The routine performance of a lateral episiotomy is advised in every case of breech delivery. Care should be used in applying suprapubic pressure on the aftercoming head.

In discussing the misuse of forceps, the author stresses the importance of avoiding cephalopelvic disproportion and misapplication of the forceps blades. The author personally favors the axis-traction type of forceps. He also warns against the use of too narrow blades.

Other causes of intracranial injury mentioned are the use of pituitrin in cases with incompletely dilated cervix and excessive manipulation in efforts at resuscitation. Here the author advises clearing the throat of mucus, traction on the tongue, injection of respiratory stimulants and administration of carbon dioxide when the infant attempts to breathe.

F. L. ADAIR AND I. C. UDESKY.

Hannah, Calvin R.: *The Prevention of Birth Injuries*, South. M. J. 28: 1021, 1935.

Quoting Ehrenfest, the author states that in many cases, especially prematures, there is extreme molding of the head causing an overriding of the bony fragments. This in turn causes a displacement of the intracranial contents, and a tearing away of veins from dural sinuses. The course of the arteries is distorted, causing occlusion resulting in anoxemia which may damage a few sensitive brain cells beyond repair. The blood vessels in the brain of a premature infant are fragile and will not resist the pressure like those of a mature baby. Therefore interruption of pregnancy should always be delayed as long as possible unless delay jeopardizes the life of the mother. Abnormal presentations and positions should be corrected before the onset of labor and thus lessen the necessity for the use of instruments. Forceps, properly applied, and a central episiotomy cause less injuries to the fetal brain than to permit the fetal head to remain on the perineum for long periods of time. Precipitate labor should be prevented by the use of sedatives or anesthesia. Fetal brain injury may be due to the failure of the brain cells to develop from faulty germ plasm rather than the fault of the delivery.

EUGENE S. AUER.

Falsia and Allievi: *Diaphragmatic Hernia of the New-Born*, Bol. Soc. de obst. y ginec. (Buenos Aires) 15: 339, 1936.

The authors present 6 cases of diaphragmatic hernia in the newborn, found at autopsy. The authors make a plea for routine autopsy in all cases of neonatal death, in order that the real diagnosis of cause of death may be made and also to exonerate the obstetrician in these cases of unavoidable death.

MARIO A. CASTALLO.

Rosenthal, S. R.: *Relationship Between Trauma Sustained at Birth and Encephalitis in Children*, Arch. Path. 16: 33, 1933.

The author reports three cases of encephalitis occurring in children of the same family, in whom the primary condition was apparently of traumatic origin at birth, while the superimposed changes were of infectious or toxic origin. The onset was insidious in all cases and characterized clinically by nervousness, vomiting and headache, so slight at first that pathologic changes in the brain were not considered. It has long been known or suggested that idiopathic and atypical cases of encephalitis in children may be caused by injuries sustained at birth. With the brain as a locus minoris resistentiae, cryptogenic or obvious infections may initiate

use of Naegele forceps of which 6 were high, 4 were midpelvic and 5 low forceps operations. In 9 of the 15 cases the forceps had been applied in the biparietal diameter. In six cases damage resulted after Kielland forceps were used. The author warns against permitting women to remain in labor for too long a time. He suggests resorting to the cervical cesarean section in cases of contracted pelvis and the avoidance where possible of the use of high forceps operations.

J. P. GREENHILL.

Lehrfeld, Louis: Limitations of Use of Silver Nitrate in Prevention of Ophthalmia Neonatorum, J. A. M. A. 104: 1468, 1935.

An elaborate survey was made in six of the largest Philadelphia hospitals in an effort to determine why ophthalmia neonatorum has not decreased. Birth records of 28,000 cases were thoroughly studied. Six hundred and thirty-two cases of ophthalmia (2.2 per cent) were found. Approximately 30 per cent of these cases were gonorrheal in origin. It appears that the Credé method of prophylaxis is not being carried out in the Philadelphia institutions as originally described by the founder or that the instillation of one drop of a germicide has been relied upon too much with a sense of complacent security.

The most striking fact of the survey is that expectant mothers known to have gonorrhea have not been actively treated for the disease. In hospitals where a careful attempt was made to treat gonorrhea before delivery the incidence of ophthalmia neonatorum was only one-fifth of that in hospitals where no attempt was made to treat the gonorrhea in the expectant mother.

The following procedures are recommended:

1. Gonorrhea in the expectant mother should be treated, not with the view of a cure, but to reduce the number of organisms present, thereby minimizing the likelihood of infection of the infant's eyes.

2. Thorough flushing of the eyes of the newborn with sterile boric acid solution, 90 c.c. being used for each eye, followed immediately by instillation of 0.5 per cent solution of silver nitrate on three successive days. On the fourth and subsequent days during the first two weeks the eyes should be flushed thoroughly with sterile boric acid solution.

3. Compulsory reporting of all cases of ophthalmia neonatorum.

4. Change in state laws to include prenatal antisepsis.

5. Superficial sterilization of the birth canal before delivery of all hospital clinic patients, particularly negroes.

GROVER LIESE.

Trattner, Sidney: Chemical Injury of Cornea in the Newborn With Report of Experiments, Virginia M. Monthly 62: 163, 1935.

Discussing corneal injuries and scars, the author states that a damage that would likely be permanent in an adult and result in loss of useful vision, often heals completely in children with little or no loss of vision. He reports a case of corneal injury in a newborn, following the use of strong silver nitrate prophylactically, so severe that no clear cornea was visible. Treatment consisted of atropine sulphate 1 per cent, cold boric irrigations and white vaseline daily. Five months later there was practically complete recovery in one eye, though less in the other.

In experimental injuries of the eyes of guinea pigs with phenol the subsequent treatments with subconjunctival injections of serum and plasma diluted with 50 per cent Tyrode's solution, an accepted ophthalmic procedure, failed to aid recovery; indeed the author believes that these subconjunctival injections rather interfered with recovery. More work on the subject is indicated.

EUGENE S. APER.

learns to breathe through the mouth. A stomach tube may be necessary to administer feedings, two or three times daily. Congenital adenoid enlargement is an important cause of nasal obstruction in the newborn.

F. L. ADAIR AND S. A. PEARL.

Gymnich, F.: *Liver Injury in the Newborn After Spontaneous Delivery*, *Monatschr. f. Geburtsh. u. Gynäk.* 91: 31, 1932.

Gymnich reviews the nine cases in the literature in which the liver in newborn babies was injured during spontaneous delivery and he reports a case of his own. The injury may consist of either a central or peripheral rupture of the liver or a subcapsular hematoma with laceration of the capsule. The cause of these injuries in spontaneous labors is pressure of the ribs against the liver. Death usually follows a few days after birth and is due to repeated hemorrhage. Prophylaxis of liver damage during labor consists of a timely episiotomy if there is difficulty in delivering the body after the head is born.

J. P. GREENHILL.

Levinson, Samuel A.: *Suprarenal Hemorrhages (Traumatic) in the Newborn*, *Am. J. Surg.* 29: 94, 1935.

In a series of 8 cases of suprarenal hemorrhages in the newborn, 6 of the infants were delivered in breech presentation. The histories were quite typical so far as there was cyanosis, dyspnea, and the infants were pallid. The labor varied from four and one-half to fourteen hours, and the mothers were multiparas. There was no previous history of an acute infection or eclampsia. The infants lived from twenty-four to twenty-seven hours after delivery. The diagnosis in most of these cases was undetermined, but in one case massive atelectasis or bronchopneumonia was suggested.

The autopsy findings were essentially negative in all the organs except for massive hemorrhage in both adrenal glands. In one of the infants was found hemorrhage in the lung parenchyma. The hemorrhage may remain within the capsule of the suprarenal gland or it may extend beyond its boundaries. The gland may become enlarged and solid, or it may undergo hemorrhagic cystic changes. At times the capsule ruptures, and the hemorrhage may infiltrate the retroperitoneal tissue. In the present series the authors have not observed any bleeding into the peritoneal cavity.

In 2 other infants, delivered by cesarean section, attempts at resuscitation were made by suspending the infant by its legs, and slapping the lumbar region, using the palm of the hand. Both these infants presented the findings already mentioned and lived twenty and twenty-eight hours, respectively. The essential pathology in these two instances was similar to that already described.

J. THORNWELL WITHERSPOON.

Schenk, F.: *The Type, Origin and Frequency of Eye Injuries in the Newborn*, *Med. Klin.* 29: 1433, 1933.

Injuries to the eye of the newborn may occur during spontaneous labor not necessarily associated with contracted pelvis or prolonged labors. In cases of contracted pelvis the incidence of these injuries is definitely greater. However, in the majority of cases, eye injuries are the result of trauma due to the pressure of forceps blades. Damage may occur not only when the blades of the forceps are applied in the occipitofrontal diameter but also when they are applied in the biparietal diameter.

In a series of 27,100 labors observed during the last twenty-one years, Schenk counted 29 instances of eye injury. Of these, 8 occurred during spontaneous labor but three of these babies presented by the face, two babies were in an occiput posterior and 3 in an occiput anterior position. Fifteen injuries resulted from the

KONSERVATIVE THERAPIE DER FRAUENKRANKHEITEN. Von Professor Dr. Heinrich Kahr, Vorstand der I. Universitäts-Frauenklinik in Wien, etc. Zweite, neubearbeitete und vermehrte Auflage. 327 Seiten. Verlag von Julius Springer, Wien, 1937.

DIE GYNAEKOLOGISCHEN OPERATIONEN. Von Professor Dr. Heinrich Martius, Direktor der Universitäts-Frauenklinik in Göttingen. 396 Seiten, mit 404, zum grössten Teil farbigen Abbildungen und Bilderreihen. Verlag von Georg Thieme, Leipzig, 1937.

THE PHYSIOLOGY AND PHARMACOLOGY OF THE PITUITARY BODY. By H. B. Van Dyke, Professor of Pharmacology, Peiping Union Medical College, Peiping, China. 577 pages. The University of Chicago Press, Chicago, 1936.

DIE KÜNSTLICHE SCHEIDENBILDUNG AUS DEM MASTDARM. Von Dr. Gotthard Schubert. 69 Seiten mit 35, teils farbigen Abbildungen. Ferdinand Enke Verlag, Stuttgart, 1936.

Items

American Board of Obstetrics and Gynecology

Practical oral and clinical examinations for Group A and B applicants will be held at Atlantic City, N. J., on June 7 and 8, 1937.

Applications for the Group A examination will be received in the office of the Secretary, Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6), Pa., to April 9, 1937. Application blanks may be secured from the Secretary's office.

Southeastern Surgical Congress

The Southeastern Surgical Congress announces the Eighth Annual Assembly of the Congress to be held in Louisville, March 8, 9, and 10, 1937, with headquarters at the Brown Hotel.

There will be three full days of postgraduate lectures and one public meeting at which time the C. Jeff Miller Lecture will be given. Its purpose is to honor the late Doctor C. Jeff Miller of New Orleans. Dr. W. D. Haggard will present the Memorial address, Dr. Frederic A. Besley, President of the American College of Surgeons, Dr. Charles Gordon Heyd, President of the American Medical Association, Dr. J. H. J. Upham, President-Elect of the American Medical Association, Dr. Frank Boland, President of the Southern Medical Association, and Dr. Fred Rankin, President-Elect of the Southeastern Surgical Congress and President of the Southern Surgical Association will all give talks on this occasion.

For information write or wire Dr. B. T. Beasley, Secretary-Treasurer, 701 Hurt Building, Atlanta, Georgia.

Correspondence

Dear Sir:

There is one statement in Dr. Tamis' article, "Management of Secondary Amenorrhea of Functional Origin" (this JOURNAL 32: 845, 1936), which requires correction.

He states, "Since then several reports have appeared substantiating these results, the latest being that of Mazer and Spitz.¹⁰ These authors stress the fact that x-ray should be a measure of last resort because of the possibility of inducing castration atrophy despite the control of dosage." There is nothing in our article which appeared in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY of August, 1935, to warrant this impression. On the contrary, in referring to eleven regularly menstruating women we state, "In none of them was the menstrual rhythm affected by irradiation in doses within the limits indicated above. This, in our opinion, is sufficient clinical proof of the safety of the procedure and discounts definitely the impression of harm when occasionally a partially amenorrheic woman incidentally passes into a more permanent state of amenorrhea following low-dosage irradiation of the ovaries." We further state: "These data indicate that the procedure is harmless."

CHARLES MAZER.

December 22, 1936.

Books Received

A PREFACE TO NERVOUS DISEASE. By Stanley Cobb, M.D., Bullard Professor of Neuropathology, Harvard Medical School, etc. 173 pages. William Wood & Company, Baltimore, 1936.

BEING BORN. By Frances Bruce Strain. 144 pages. D. Appleton-Century Company, New York, 1936.

RADIOTHÉRAPIE GYNÉCOLOGIQUE. Par R. Mathey-Cornat, Radiologiste des hôpitaux, etc. 369 pages. Masson et Cie, Paris, 1936.

MEDICAL DICTIONARY. By Thomas Lathrop Stedman, A.M., M.D. Thirteenth revised edition, illustrated, 1291 pages. William Wood & Company, Baltimore, 1936.

YEAR BOOK. Royal Prince Alfred Hospital Medical Officers' Association. Sydney, N. S. W., 1935.

MEDICAL CLASSICS. Compiled by Emerson Crosby Kelly, M.D., Department of Surgery, Albany Medical College. The Williams & Wilkins Co., Baltimore, 1936.

A TEXTBOOK OF OBSTETRICS. By Edward A. Schumann, M.D., F.A.C.S., Professor of Obstetrics, School of Medicine, University of Pennsylvania, etc. 780 pages with 581 illustrations. W. B. Saunders Company, Philadelphia, 1936.

THE MANAGEMENT OF OBSTETRIC DIFFICULTIES. By Paul Titus, M.D., Obstetrician and Gynecologist to the St. Margaret Memorial Hospital, etc. 879 pages, with 314 illustrations, including four in color plates. The C. V. Mosby Company, St. Louis, 1937.

The importance of the interplay between all the hormones is being realized more and more. For this reason our studies can be evaluated as covering only two of many factors in a complicated equation. Notwithstanding the limitations of the present technic of assay, we have found that the prolactin and estrin of the blood and urine follow remarkably consistent curves throughout normal pregnancies, and have also detected unmistakable variations from these curves in cases of late pregnancy toxemia, exclusive of nephritis. Whether or not any etiologic significance may be attached to these variations, can for the present be only a matter for conjecture. They do suggest possible therapeutic approaches.

Assays for these two hormones in the blood and urine of 69 pregnant women and in 26 placentas have already been reported.¹⁻⁴ Thirty-eight per cent of the cases were normal, 42 per cent had mild to severe preeclamptic toxemia and 20 per cent had eclampsia. The results indicated that excessive amounts of prolactin and a tendency toward low levels of estrin were characteristic of the toxemias (exclusive of nephritis) and that this abnormality was of placental origin.

One patient, from whom repeated specimens were analyzed during gestation, showed an abnormal rise in serum prolactin two months before the development of clinical toxemia. A single specimen of serum from another patient contained high prolactin; a month later toxemia appeared. We were especially interested in confirming this last finding. Since the incidence of late pregnancy toxemia is high in diabetics, the study of these cases seemed to offer the best chance of being able to ascertain whether or not toxemia might be detected before it becomes clinically manifest.

In this paper are presented curves of prolactin and estrin based on the study of 27 pregnant women, 11 with diabetes, from as early as possible in gestation to delivery. Six patients, four of them diabetics, developed preeclamptic toxemia. Seventeen, including five diabetics, went through uneventful pregnancies and were delivered of normal, living infants. The remaining four pregnancies were neither strictly normal nor yet frankly toxemic and will be considered separately.

The method used in quantitating prolactin in urine and serum has been the same as that previously described.²

In assaying serums, urines, and placentas for prolactin (A.P.L.), a double end-point phenomenon has been encountered and deserves mention. We have considered the smallest amount of material, extracted and administered by the Aschheim-Zondek technic to immature rats, nineteen to twenty-one days old, which produces grossly visible discrete corpora lutea by the ninety-sixth hour the prolactin end-point. Often, however, a second end-point appears: e.g., extracts of 2.0 c.c., 1.5 c.c., and 1.0 c.c. of a given serum give corpora lutea, while 0.7 c.c., 0.5 c.c. and 0.3 c.c. result grossly in the so-called A effect, cystic uterus, and follicle ripening; but in the rats receiving 0.2 c.c. and 0.1 c.c. corpora are again found. In other words,

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Original Communications

PROLAN AND ESTRIN IN THE SERUM AND URINE OF DIABETIC AND NONDIABETIC WOMEN DURING PREGNANCY, WITH ESPECIAL REFERENCE TO LATE PREGNANCY TOXEMIA*

O. WATKINS SMITH, PH.D., AND GEORGE VAN S. SMITH, M.D.,
BROOKLINE, MASS.

WITH THE COOPERATION OF ELLIOTT P. JOSLIN, M.D., AND
PRISCILLA WHITE, M.D., BOSTON, MASS.

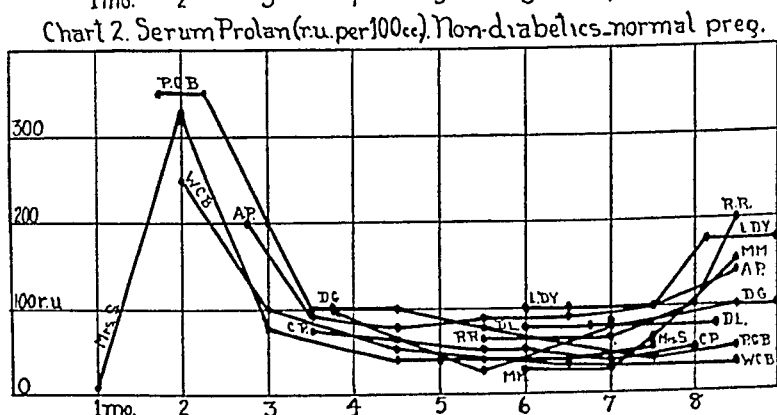
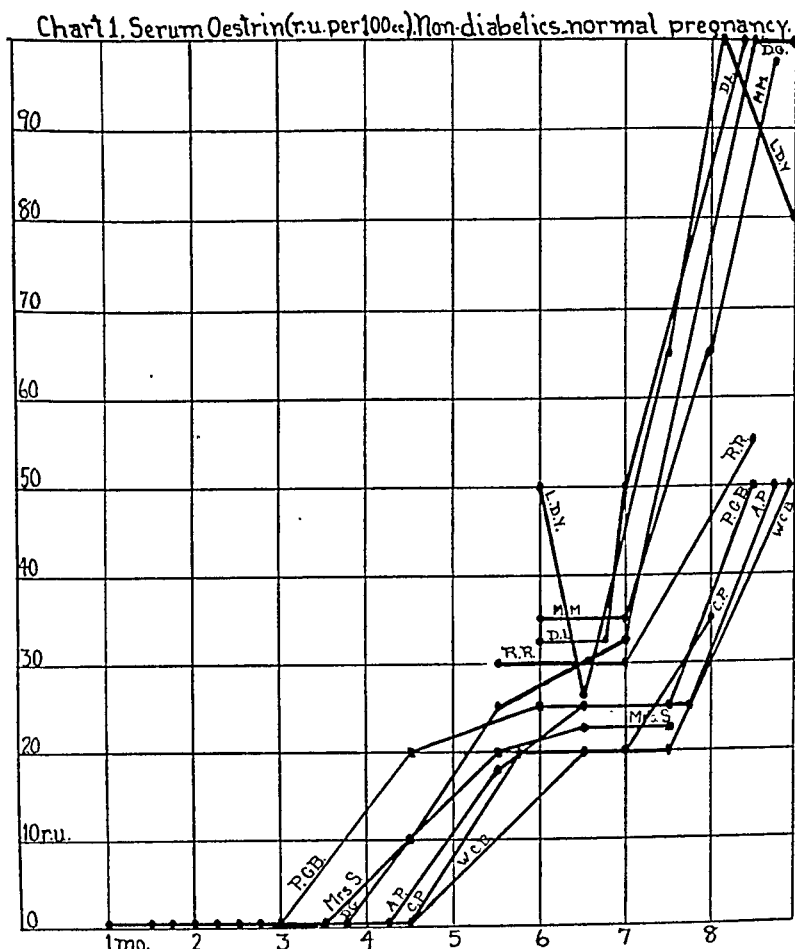
*(From the Fearing Research Laboratory, Free Hospital for Women, Brookline, Mass.,
and The George F. Baker Clinic of the New England Deaconess
Hospital, Boston)*

ALTHOUGH careful studies have revealed certain biochemical variations from the normal in the blood and urine during pregnancy, none is as striking, from a quantitative point of view, as the hormonal changes thus far demonstrated; namely, in the amounts of the anterior pituitary-like, gonad-stimulating factor (prolan of placental origin) and estrogenic substances (estrin). Undoubtedly there are marked endocrine changes associated with other organs besides the placenta as indicated morphologically (e.g., pituitary, ovaries, adrenals, and thyroid), but the analysis of blood and urine by any methods approaching quantitative standards is still limited to prolan and estrin, and even with these the shortcomings of existing procedures render the results only approximately accurate.

*Read before the Section on Obstetrics and Gynecology, New York Academy of Medicine, November 26, 1935.

The Mrs. William Lowell Putnam Investigation of the Toxemias of Pregnancy.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."



Charts 1, 2, 3, and 4.—Nondiabetics, normal pregnancies. All but two of these patients went through uneventful pregnancies and had normal deliveries at term.

Mrs. S. spontaneously ruptured her membranes and delivered a premature infant at seven and one-half months. Her prolactin and estrin curves did not differ from the normals, other than in a tendency towards low estrin levels.

Mrs. L. D. Y. began having severe uterine cramps at five and one-half months. At six months, it being apparent that both serum and urinary estrin were abnormally high, she was given 600 rat units of antophysin (Winthrop Chemical Company's A.P.L. preparation) and 21 rabbit units of proluton (Schering Corporation's progestin) during the course of ten days. This was followed by a drop in the estrin level in both serum and urine. The clinical benefit of the treatment was doubtful, for, although the cramps were less severe following injections, they recurred intermittently from six and one-half months to delivery, which was at full term and normal. The last blood specimen on this patient, and also on Mrs. D. G., was taken during labor.

the serum might be considered to contain either 100 or 1000+ R.U. per 100 c.c. Davy, comparing the weights of ovaries at various injection levels, reports a similar observation.⁶

The first corpus luteum end-point values have formed uniform curves throughout normal pregnancies. The second end-points have been most inconsistent, being entirely absent in some specimens and in others giving results up to 30 times those indicated by the first end-point. No relationship could be established between the second end-point findings and the time of gestation or the condition of the patient.

We are at a loss to explain adequately this phenomenon. Probably stimulation of the rats' own hypophyseal luteinizing hormone by the estrin of the follicle ripening produced by smaller amounts of A.P.L. plays a part in giving the second appearance of corpora.⁷ The prolan A effect with the larger quantities of A.P.L. may in some way be associated with antibodies, either in the extracts themselves or in the rats, due to the injected material.^{8, 9} It is also likely that this phenomenon is related both to the number and time of injections, and to the amount given each time. Since the second end-point appears to be involved in more complex interactions, it seems advisable to present our results in terms of the first end-point figures.

For the determination of urinary estrin we have employed acid hydrolysis of specimens prior to extraction or assay,⁵ since this method yields such high and apparently reliable values (see Charts 3 and 7).^{*} The placentas of 8 of the diabetic patients have been analyzed for prolan and estrin by the same technic as that previously reported.⁴

EXPERIMENTAL RESULTS

Charts 1, 2, 3, and 4 summarize in graph form the data collected on the normal nondiabetic pregnancies. In 1927 Margaret Smith reported a constant increase in whole blood estrin from early in pregnancy to delivery.¹⁰ During the first three months of normal pregnancy we have been unable to demonstrate estrin in 10 c.c. of serum. The urinary estrin (hydrolyzed urines) has never amounted to more than 5,000 R.U. in twenty-four hours. From then on, the level of estrin in both serum and urine increases, the most rapid and marked rise being apparent during the last trimester. The values for urinary estrin given by unhydrolyzed specimens are included in the chart to demonstrate the inadequacy of assaying untreated urine. Smith reported a marked increase in whole blood estrin during and shortly before labor. In two of our cases, Mrs. L. D. Y. and Mrs. D. G., the serum estrin level was found to be no higher during labor than two to four weeks earlier. Mrs. L. D. Y.'s serum actually contained less one-half hour before delivery than at the eighth month (and the estrin content of her amniotic fluid was the same as that of the serum). It may well be that the partition of estrin between cells and serum changes.

^{*}The high "total" estrin content of urines from women over three months pregnant makes extraction of the hydrolyzed specimens unnecessary. Five or 10 c.c. (depending upon the period of gestation and the twenty-four-hour volume) are measured into a 200 c.c. volumetric flask. Fifteen volumes per cent of concentrated HCl are added and the flask heated inside the steam bath (temp. 100° C.) for one hour. The contents are diluted to volume with water, mixed, and tested directly on the rats.

Chart 5. Serum Oestrin (r.u. per 100 cc.) Late pregnancy toxæmia.

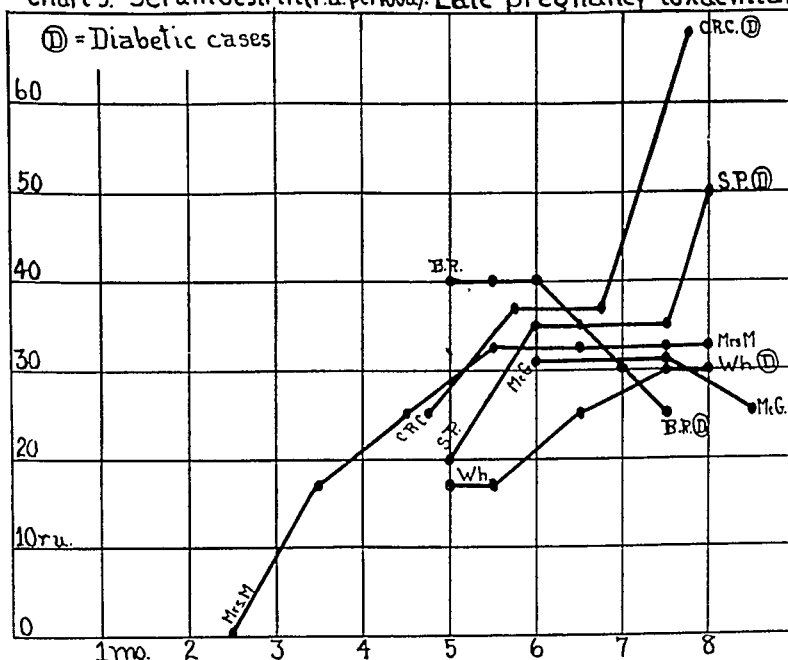
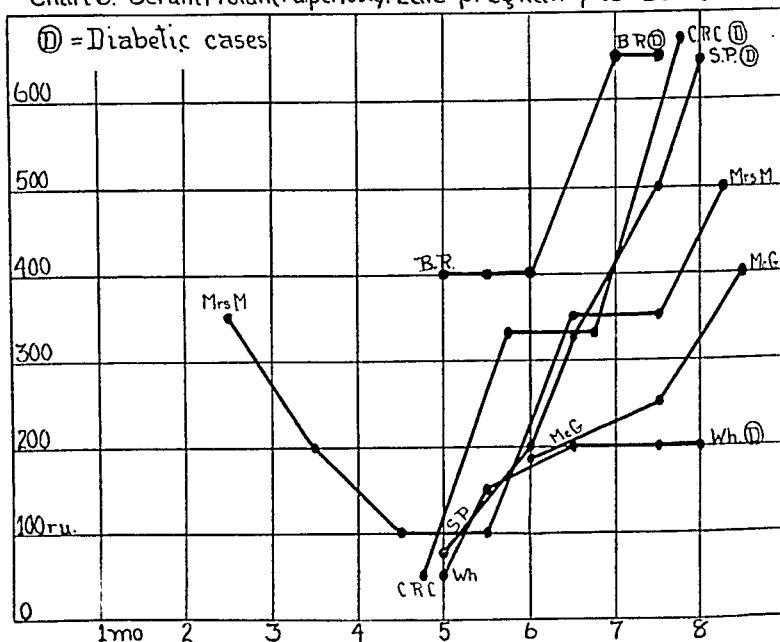


Chart 6. Serum Prolan (r.u. per 100 cc.) Late pregnancy toxæmia



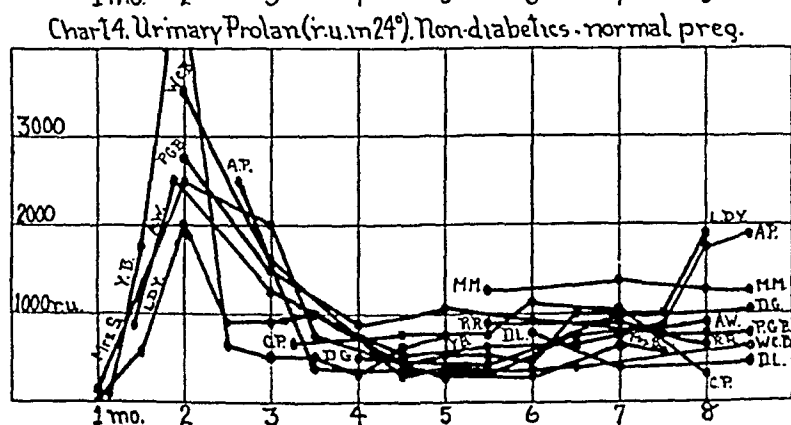
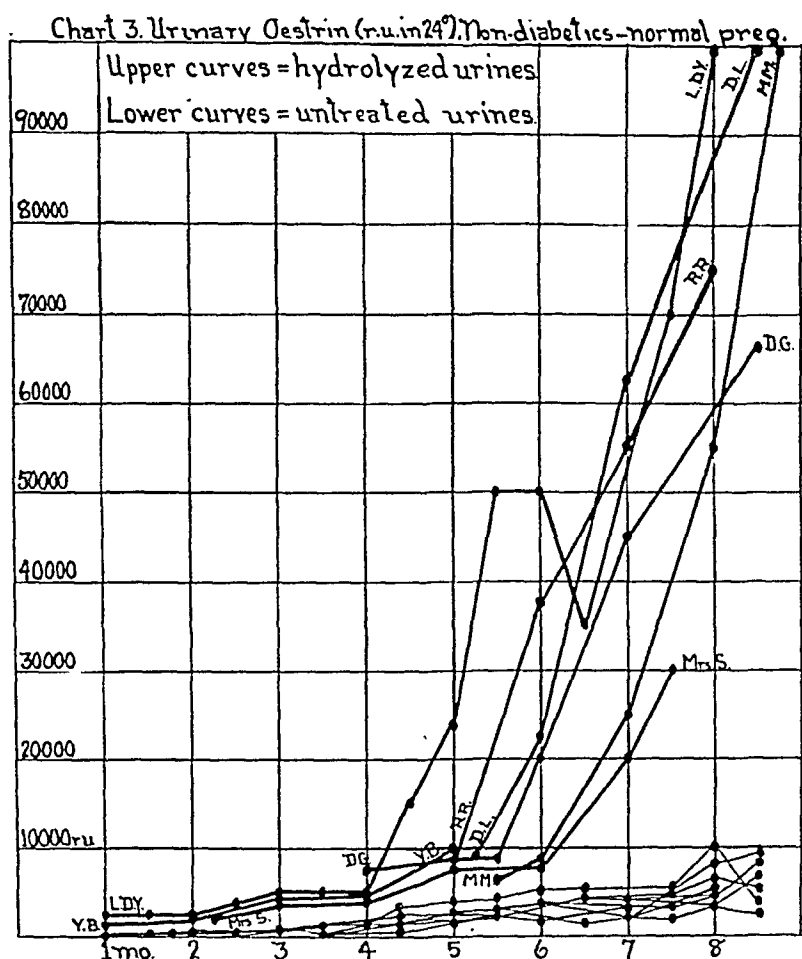
Charts 5, 6, 7, and 8.—Cases of late pregnancy toxæmia.

Mrs. M. (Nondiabetic.) Clinically normal to the beginning of the eighth month; then slightest possible trace of albumin in urine. At eight and one-half months, blood pressure 140/90; albumin, trace; edema, +++ Induced delivery one week before term of a normal, living infant.

Mrs. McG. (Nondiabetic.) At seven and one-half months, blood pressure, 140/90; otherwise normal. At eight and one-half months, blood pressure, 150/110, albumin, slight trace; edema, +++. Normal delivery of a normal, living infant ten days before term.

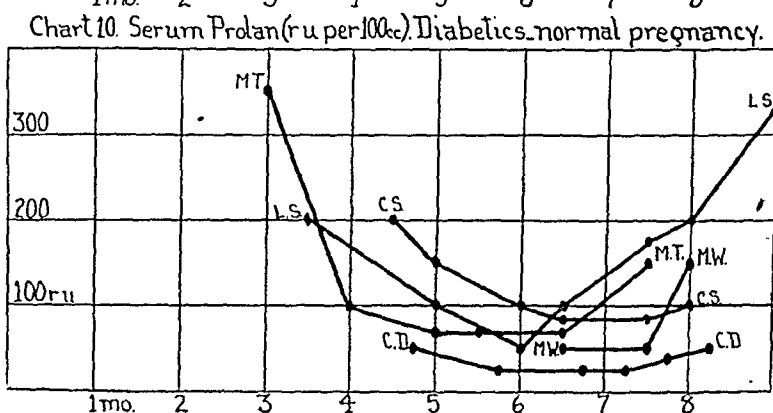
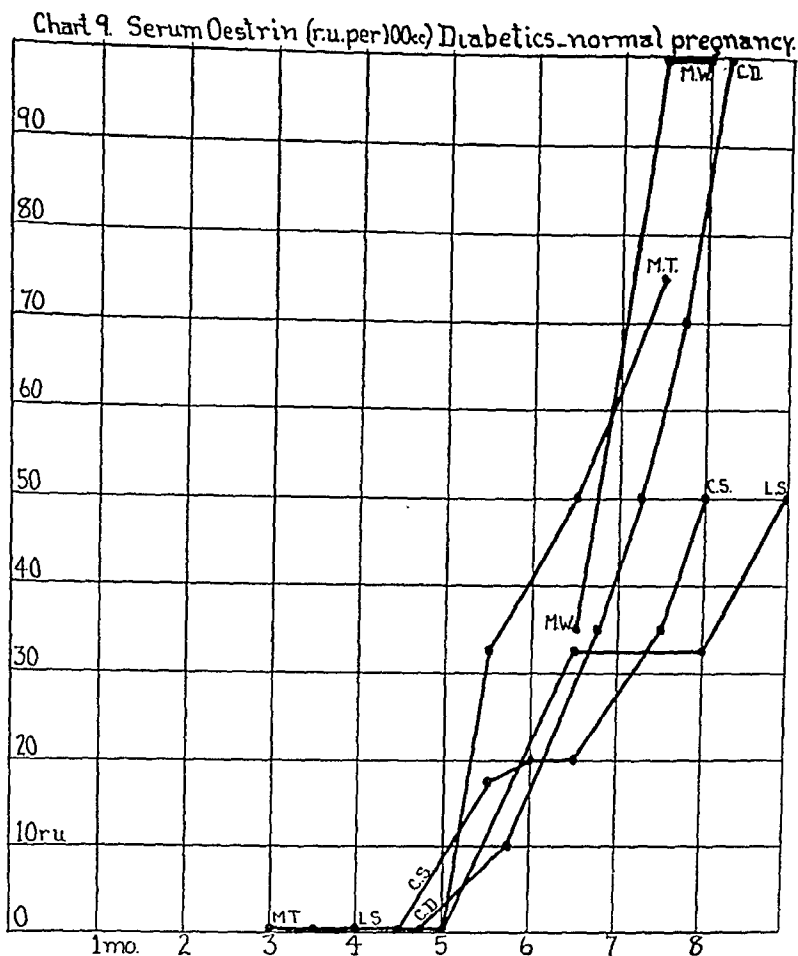
Mrs. S. P. (Diabetic.) Diabetes well controlled throughout pregnancy with 35 to 50 U. insulin daily. Slight edema at seven months; otherwise normal. At eight months, blood pressure, 140/80; albumin, trace; edema, +++. Early in the eighth month a ten and three-fourths pound, edematous infant was delivered by cesarean section.

(Continued on opposite page.)



In 1928 Zondek¹¹ reported that prolan reached its highest level between the second and fourth month and from then on decreased moderately to delivery. The analyses of both serum and urine in our series of normals revealed a peak in prolan at about two months. By the beginning of the fourth month the prolan had dropped to a comparatively low level, which was maintained to the last month of pregnancy when, in several cases, a rise was apparent.

Charts 5, 6, 7, and 8 present the prolan and estrin curves on the two nondiabetic and the four diabetic women who developed preeclamptic toxemia. In four of these, in contrast with the normals, the serum estrin did not rise during the last two months. In the only three cases



Charts 9, 10, 11, and 12.—Diabetics, normal pregnancies.

Mrs. M. T. Diabetes well under control throughout pregnancy with 35 to 50 U. insulin daily. Intermittent nausea and vomiting during first five and one-half months. (Note rise in estrin coincident with cessation of nausea.) Delivered by cesarean section early in the eighth month of a normal, 6 pound 6 ounce infant.

L. S. Very mild diabetes; no insulin required. Normal delivery at term of a 5½ pound, living infant.

Mrs. C. S. Diabetes well controlled throughout gestation with 30 to 60 U. insulin daily. Delivered by cesarean section early in the eighth month of a normal, 8 pound, living infant, which died three hours later. Autopsy diagnosis: prematurity.

Mrs. M. W. Diabetes controlled with 50 U. insulin daily. Delivered by cesarean section early in the eighth month of a normal, 5 pound, living infant.

Mrs. C. D. Diabetes impossible to control; 80 U. insulin a day. Delivered by cesarean section early in the eighth month of a normal, 6 pound 11 ounce, living infant. Hydramnios.

Chart 7. Urinary Oestrim (r.u. in 24) Late pregnancy toxæmia.

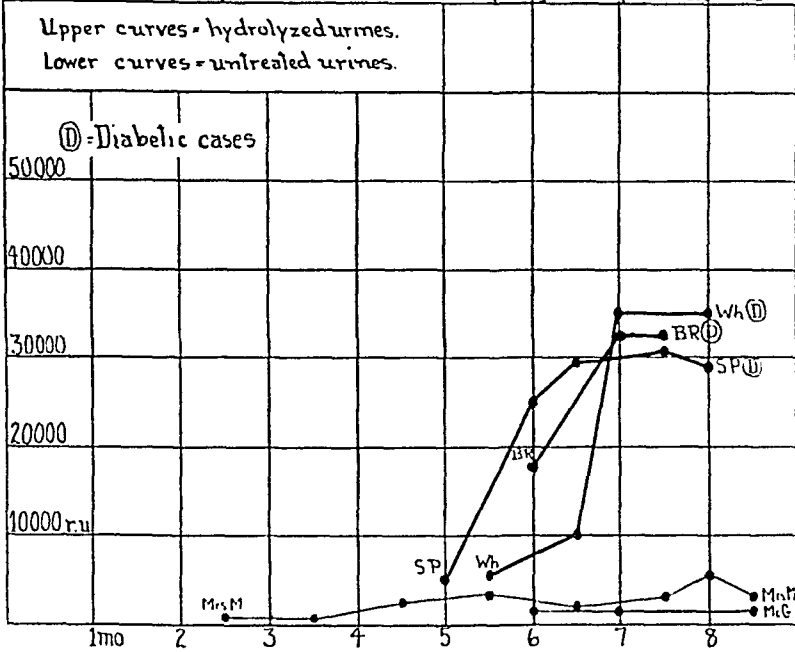
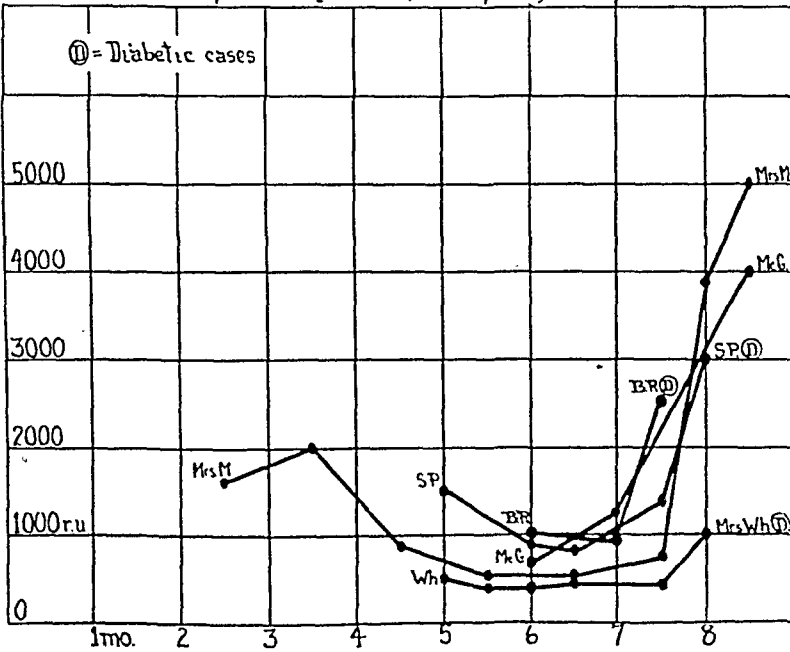


Chart 8. Urinary Prolan (r.u. in 24) Late pregnancy toxæmia.



Mrs. Wh. (Diabetic.) Diabetes well controlled throughout pregnancy with 50 U. insulin daily. At seven and one-half months slight edema and slightest possible trace of albumin; otherwise normal. At eight months, blood pressure, 160/110; albumin, large trace; edema, +++. The last specimen was taken one day before the death of the fetus, which event was followed by cessation of toxemia. Delivery of a large macerated fetus occurred five weeks later.

Mrs. C. R. C. (Diabetic.) Diabetes fairly well controlled with 40 U. insulin daily. No symptoms of toxemia until end of seventh month. Then, within a few days, blood pressure, 160/110; albumin, very slight trace; edema, +++. Delivered immediately by cesarean section of a fat but not typically edematous infant weighing 6 pounds and 13 ounces.

Mrs. B. R. C. (Diabetic.) Severe diabetes well controlled with 20 to 60 U. insulin daily. Slight rise in blood pressure and a trace of albumin at seven months. At seven and one-half months, blood pressure, 172/104; albumin, large trace; edema, +++. Delivered by cesarean section of a normal infant weighing five pounds and five ounces.

Chart 13. Serum Oestrin (r.u. per 100 cc.) Abnormal cases.

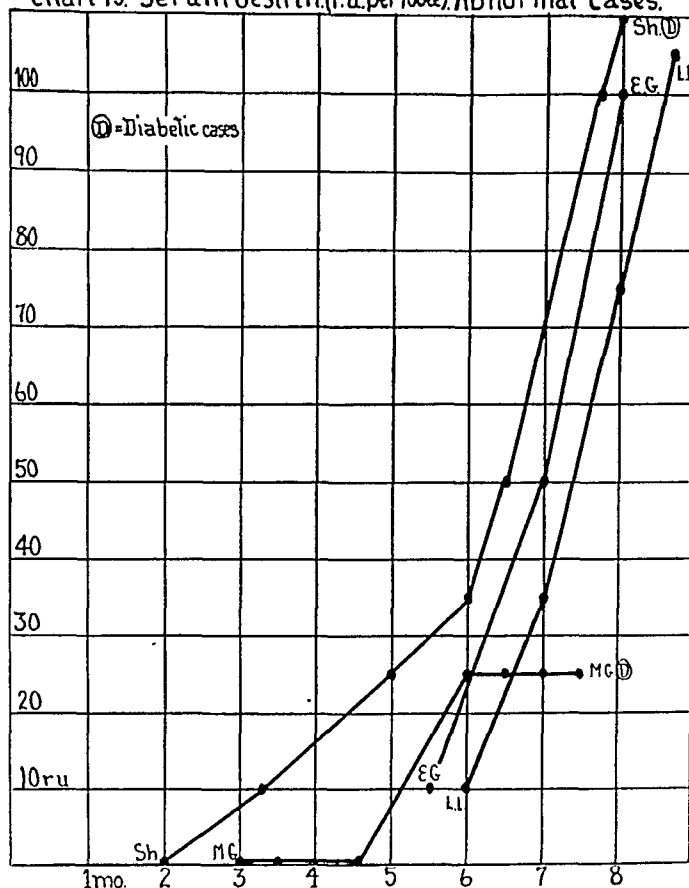
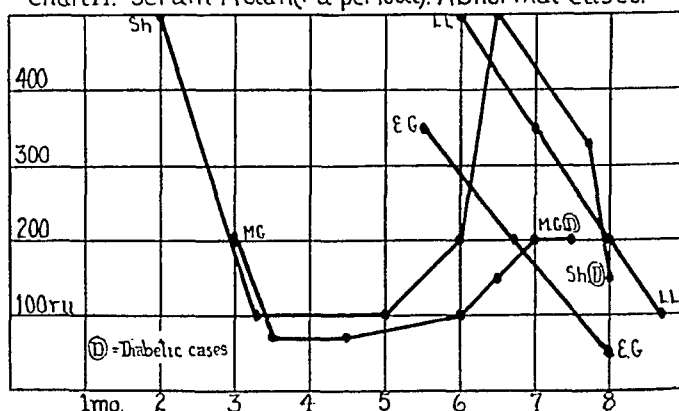


Chart 14. Serum Prolan (r.u. per 100 cc.) Abnormal cases.



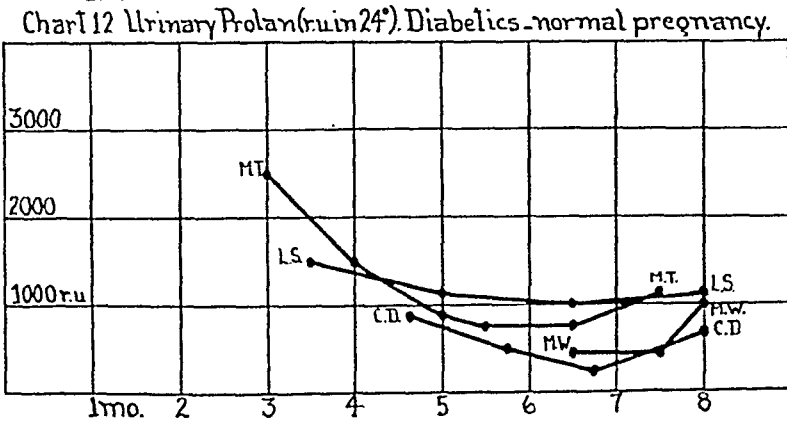
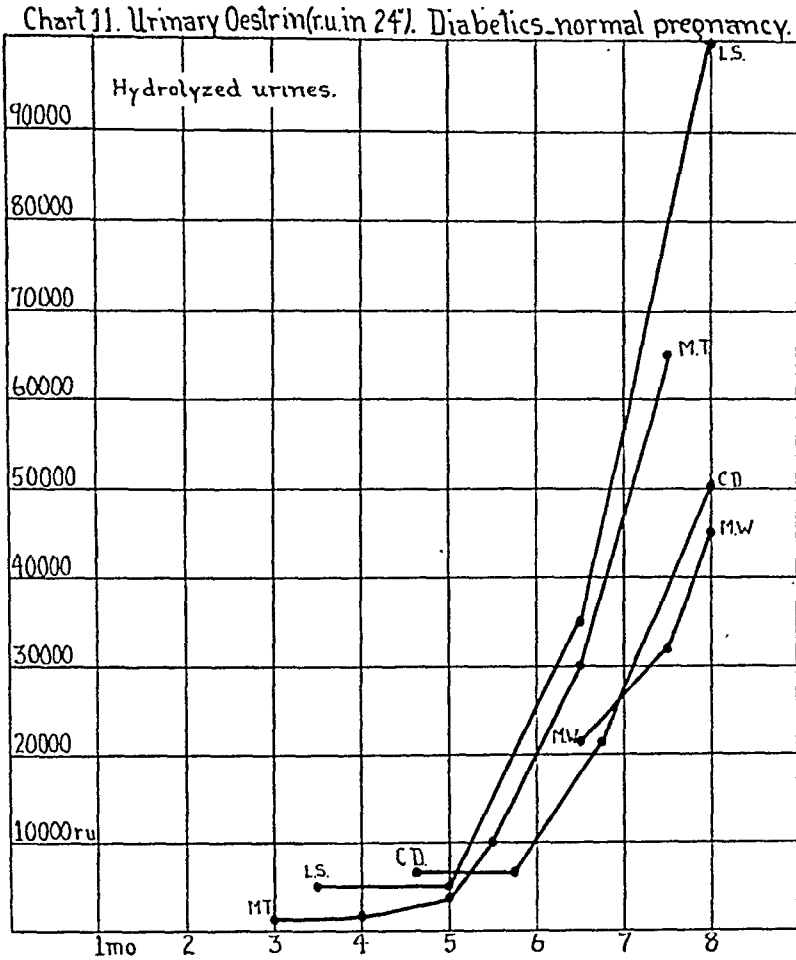
Charts 13, 14, 15, and 16.—Four abnormal cases.

Mrs. M. G. (Diabetic.) Diabetes well controlled throughout gestation with 8 to 28 U. insulin daily. Hydramnios but no signs of toxemia. At seven and one-half months spontaneous premature delivery of a 7½ pound, edematous, giant infant, which lived only twenty minutes. Autopsy revealed hemorrhagic disease, rickets and scurvy.

Mrs. Sh. (Diabetic.) Diabetes controlled with 20 U. insulin per day. At eight months a large trace of albumin appeared in the urine; otherwise clinically well. Delivered early in the eighth month of an 8½ pound, edematous, giant infant.

E. G. (Nondiabetic.) Normal gestation until the middle of the seventh month, when a trace of albumin appeared in the urine. This continued until delivery, which was full term and normal. No other signs of toxemia.

L. L. (Nondiabetic.) Normal pregnancy except for a rise in blood pressure during the last month to 158/80. Delivery was at full term and normal.



whose urines were assayed after hydrolysis, the excretion of estrin failed to increase after the seventh month. These estrin abnormalities were not demonstrable until shortly before the appearance of toxemia.

The serum prolan of all these cases began to rise during the second trimester and at no time after the beginning of the sixth month was it less than 200 R.U. per 100 c.c. These curves contrast markedly with the normal in which, without exception, the serum prolan from the fourth to the eighth month was 100 R.U. or less per 100 c.c. The rise in serum prolan was apparent in each case of late pregnancy toxemia at least six weeks before the clinical diagnosis could be made. Prolan

edematous, giant infant. The second, Mrs. Wh., delivered a large macerated fetus five weeks after it had died. Mrs. C. R. C., the third, was delivered by cesarean section shortly before the eighth month because a rise in blood pressure and marked edema suddenly developed. The living infant was large but not typically edematous. Mrs. B. R. was delivered at seven and one-half months by cesarean section of a five-pound, normal, living baby.

Charts 9, 10, 11, and 12 contain the curves on five diabetic women who went through pregnancy without accident and were delivered (four by cesarean section) of normal, living infants. In general the prolactin and estrin levels follow the same curves as those for the non-diabetic normals. There is a tendency, however, toward a later drop in serum prolactin, a later appearance of demonstrable serum estrin, and an earlier and more pronounced rise in the serum prolactin toward term. In other words, the curves vary slightly from the normal nondiabetic in such a way as to suggest that they approach the toxemic borderline. This departure may be linked with the high incidence of toxemia in diabetic pregnancies.

Two diabetic patients, not included in the charts, had premature deliveries immediately after the first specimens were taken, one at six and the other at seven months. Neither had toxemia and their babies were not edematous. Their prolactin and estrin levels were within the limits of normal. Among the few nondiabetic cases of miscarriage and premature delivery that we have studied, no typical prolactin or estrin abnormalities have been evident.

Charts 13, 14, 15, and 16 present the analyses on four women who could not be grouped either as definitely toxemic or strictly normal. In all of them the appearance of excessive serum prolactin at five to seven months led us to predict late pregnancy toxemia.

Mrs. M. G., diabetic, delivered a premature, markedly edematous infant at seven and one-half months. She had a hydramnios but no clinical evidence of toxemia. Both prolactin and estrin curves were entirely comparable with those of the toxemics.

Mrs. Sh., diabetic, showed a rise in prolactin at six months and a high level at seven months, but her estrin was rising too. At eight months a large trace of urinary albumin appeared. However, between the seventh and eighth month the prolactin decreased and her estrin rose markedly. Albuminuria continued to delivery, but there was no other evidence of toxemia. Her infant was a typical diabetic giant.

E. G. and L. L., two nondiabetics, showed curves entirely similar to those of Mrs. Sh., i.e., high prolactin near the sixth month followed by a drop coincident with a marked increase in estrin. E. G. had only albuminuria; L. L. had a rise in blood pressure. Both delivered full-term, normal, living infants.

From the results demonstrated in the first twelve charts, our interpretation of these four cases would be that Mrs. M. G. might have developed toxemia had pregnancy continued; whereas in the other three the rise of estrin and drop in prolactin after the seventh month may have been associated with the fact that clinically there was only mild toxemia.

Chart 15. Urinary Oestrin (r.u. in 24) Abnormal cases

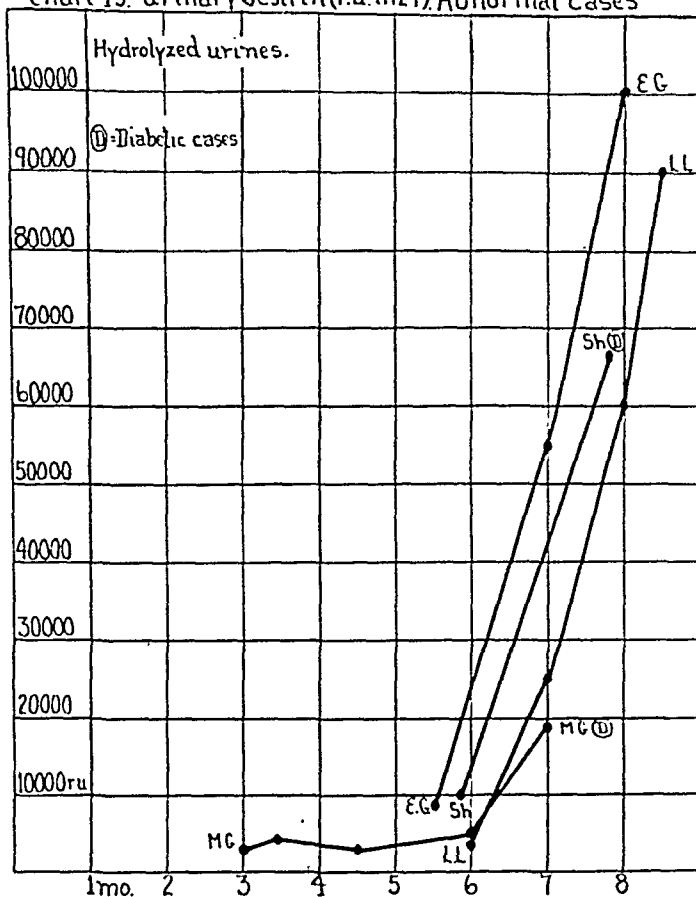
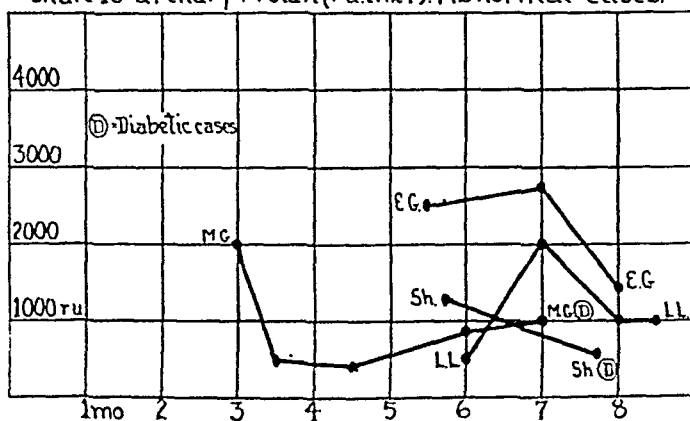


Chart 16 Urinary Prolan (r.u. in 24) Abnormal cases.



excretion was high in four of the five patients whose urines were assayed, but not until the clinical diagnosis had been made. This lag in prolan excretion in the toxemies seems to us to be of especial interest and importance, since in all the other curves the prolan and estrin levels for serum and urine run roughly parallel. There was no variation of the prolan or estrin findings in the four toxemic diabetics that might differentiate them from the nondiabetic cases with toxemia.

Mention should be made of these patients' infants. The two nondiabetic patients had normal, living babies. Of the diabetics, Mrs. S. P. was delivered by cesarean section early in the eighth month of a ten and three-fourths pound, living,

that the administration of large amounts of estrin resulted in a temporary lowering of prolactin. Although our present state of knowledge does not justify the assumption of high prolactin as an etiologic factor in the toxemias of late pregnancy, the results presented do point toward estrin as an experimental therapeutic measure.

In a previous communication⁴ we advanced the hypothesis that toxemia might be the result of a diffuse and vicarious menstrual-like process occurring in pregnancy. Clinically the analogy is weak. Mild to severe edema or an increase in weight at the time of menstruation has been reported. The various disturbances at menstruation reflect an upset of the sympathetic nervous system. (In this category also could be included cases of functional bleeding, especially menopausal.) The above hypothesis was suggested by our hormonal studies from which we now associate the onset of toxemia with high prolactin and relatively low estrin. The consensus of opinion is that both normal menstruation and functional bleeding in women and experimental bleeding in monkeys follow a drop in estrin. In nine out of ten instances we have found a rise in urinary prolactin (probably hypophyseal) before or at menstruation. Moreover, increased prolactin (probably hypophyseal) has been reported in a large percentage of women with functional bleeding.^{14, 15} The analogy is strengthened by the pathology of toxemia, which is characterized by changes due to and associated with edema, necrosis, and capillary thrombosis and hemorrhage, all of which processes point to arteriolar spasm as the common denominator,¹⁶ and this in turn implicates the sympathetic nervous system. Edema, necrosis, capillary thrombosis, and hemorrhage are typical findings in the endometrium at menstruation and are in part characteristic of the endometrium of functional bleeding. It has recently been announced¹⁷ that arteriolar spasm initiates the endometrial bleeding of monkeys. From these pathologic considerations the theory seems tenable that cases of toxic separation of the placenta are the result of actual menstruation during pregnancy, while toxemia might well be due to the same process taking place vicariously rather than in the endometrium alone.

This theory suggests another therapeutic approach. Menstruation has been inhibited in monkeys¹⁸ by the giving of sufficient progesterin. There is growing evidence that human menstruation can be prevented by progesterin. The possibility of progesterin therapy in late toxemia is, therefore, appealing.

We are now attempting to compare the progesterin content of placentas from normal and toxemic cases, but, although the hormone can be identified in this organ, the present methods of assay are not sensitive enough to make comparative analyses significant.

SUMMARY

Analyses on 12 nondiabetic women throughout normal pregnancies indicate that the peak in prolactin of both urine and serum occurs at approximately two months and that by the beginning of the fourth month this hormone reaches a lower and fairly constant level coincident with an increase in estrin. The most rapid rise in estrin of both urine and serum takes place during the last trimester.

The data on 6 cases of late pregnancy toxemia (4 of them diabetics) confirm the previously reported finding of high prolactin and low estrin in this condition and demonstrate that *the abnormal rise in serum prolactin precedes the clinical manifestations by at least six weeks.*

The curves on 5 diabetic women throughout normal pregnancies are essentially similar to those of the normal nondiabetics. A somewhat later rise in estrin and a less marked plateau of prolactin suggests, how-

In Table I are analyses of the placentas from eight of the diabetic cases. As was found in nondiabetic pregnancies,⁴ the placental figures confirm the blood and urinary findings and indicate also that excessive prolan is of placental origin. The analyses of Mrs. Wh.'s placenta are included to demonstrate that prolan and estrin persisted even after death of the fetus. The values, however, are presumably lower than they were when the fetus was alive and the patient toxemic.

TABLE I. PROLAN AND ESTRIN IN THE PLACENTAS FROM 8 DIABETICS

CASE	CLINICAL DATA	PROLAN R.U. PER G. (DRY WT.)		ESTRIN R.U. PER G. (DRY WT.)	
		MA- TERNAL	FETAL	MA- TERNAL	FETAL
Mrs. E. D. ¹	Miscarried at 6 months No toxemia Baby not edematous	2.0	3.0	6.0	10.0
Mrs. E. W. ¹	Miscarried at 7 months No toxemia Baby not edematous	3.0	4.5	15.0	15.0
Mrs. M. W. ²	Normal pregnancy Cesarean at 8 months Baby not edematous	4.5	2.0	6.0	10.0
Mrs. M. T. ²	Normal pregnancy except for early nausea Cesarean at 8 months Baby not edematous	3.0	6.0	15.0	10.0
Mrs. C. S. ²	Normal pregnancy Cesarean at 8 months Baby not edematous	3.0	4.5	10.0	15.0
Mrs. S. P. ³	Late pregnancy toxemia Cesarean at 8 months Baby typical diabetic giant	45.0	60.0	6.0	3.0
Mrs. M. G. ⁴	Miscarried at 7½ months No toxemia. Hydramnios Baby typical diabetic giant	18.0	30.0	7.5	6.0
Mrs. Wh. ³	Late pregnancy toxemia Baby died 5 weeks before de- livery	6.0	6.0	5.0	5.0

¹Urinary and serum values not included in charts, well within the limits of normal.

²For urinary and serum values, see Charts 9, 10, 11, and 12.

³For urinary and serum values, see Charts 5, 6, 7, and 8.

⁴For urinary and serum values, see Charts 13, 14, 15, and 16.

DISCUSSION

One of the most striking features of these charts is the fact that high levels of serum prolan are almost invariably associated with low estrin and vice versa. In the normal pregnancies estrin was not demonstrable in 10 c.c. of serum until the prolan had dropped from the two-month peak. In the toxemias the abnormal rise in serum prolan was followed by a leveling-off or drop in serum estrin during the last trimester, at which time the normal curves showed their greatest estrin rise. The diabetics who went through pregnancy normally showed a somewhat later drop in serum prolan than the nondiabetic normals, together with a later appearance of demonstrable serum estrin. The mutually antagonistic action of these two hormones is particularly indicated in the three cases of very mild toxemia presented in Charts 13, 14, 15, and 16. We have previously demonstrated that the administration of prolan (A.P.L.) to pregnant women resulted in a temporary lowering of the level of estrin.¹² We have also, in two cases (Case 21.² and Case 1.¹² found

DIABETES COMPLICATING PREGNANCY*

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THE unfavorable effects of diabetes complicating pregnancy are manifested by: (1) accidents to the fetus; (2) maternal toxemia and eclampsia; (3) maternal coma; (4) maternal hypoglycemia. Our own medical conception of this problem is based upon an analysis of 271 pregnancies which have occurred in 191 diabetic women consulting Dr. Joslin between 1898 and October, 1935. Approximately half of these cases occurred in the preinsulin and one-half in the insulin eras. A comparative analysis of these two periods shows surprisingly slight improvement, for stillbirths have dropped only from 29 to 25 per cent, miscarriages and abortions from 22 to 16 per cent. We are, therefore, naturally concerned with the investigation of the manner in which diabetes appears to contribute to these accidents and in that form of treatment of the disease which most successfully avoids them.

Early abortion and miscarriage we attribute directly to a lack of control of diabetes, for their incidence was some six times greater among cases characterized by elevation of the blood sugar and glycosuria than among those patients who had more adequately controlled diabetes. Although positive evidence of such important theoretical factors as deficiency diet, a lethal factor in the primary cell, endocrine imbalance early in pregnancy, acidosis and hypoglycemia were lacking in this series, they need further investigation. The characteristic pathology of uncontrolled diabetes seems to us, however, to indicate how harmful it may be. It is known that the impregnated ovum implants itself in that portion of the uterus which has the richest supply of glycogen. Failure of the normal deposition of glycogen is a characteristic lesion of uncontrolled diabetes, and this lack of glycogen should theoretically favor imperfect nidation.

Toxemia and eclampsia occur nearly fifty times more frequently in the diabetic than they do in the nondiabetic childbearing population at large. These conditions are more common in the younger and, consequently, the severer cases. The severity of diabetes rather than its control favors the development of these complications. That toxemia may be the consequence of diabetes is indicated by the newer physiologic research which seems to show that toxemia is associated with an abnormal hormonal state probably related to the placenta, that diabetes is a disease of interglandular relationships and that there are other similar

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ever, that the high incidence of toxemia in diabetic pregnancies may be linked with a prolan-estrin imbalance which approaches the toxemic borderline.

In 4 cases, two diabetic patients, high serum prolan at five to seven months led to the prediction of late pregnancy toxemia. One of these women (diabetic) had a premature delivery at seven and one-half months. The other 3 showed a very marked rise in estrin during the last trimester coincident with a drop in prolan to within the limits of normal and the appearance of only very mild toxic symptoms.

Of the 11 diabetic patients followed, 4 had either stillbirths or edematous giant infants. All 4 of these women showed the prolan-estrin imbalance typical of toxemia at five to seven months. The diabetic patients with normal curves for prolan and estrin delivered normal, living infants. Two of the diabetic patients, on the other hand, whose prolan was excessive and who developed severe toxemia, were delivered by cesarean section at seven and one-half months of normal, living infants. Although it might be argued that in these two cases early delivery had preceded abnormal growth of the fetus, the data at hand are too limited to permit the establishment of any connection between the endocrine findings and the type of infant in diabetic pregnancies.

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The author reviews the literature on the subject of ovarian transplants.

Autotransplantation of ovaries of rabbits into the anterior chamber of rabbits' eyes provides an excellent method for research as it permits perfect visualization of the transplant during its period of activity. Unilateral transplants do not function and soon disappear. Bilateral transplants, however, grow without much difficulty. After maturation, two kinds of follicles develop, one with a very short cycle and the other, a persistent follicle, becomes cystic and does not respond typically to gonadotrophic stimuli. Administration of large amounts of estrogenic hormone failed to cause rupture of the follicles except in one case where a rupture of the tissues had occurred with protrusion of the follicle. The article is beautifully illustrated with colored plates.

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once with a perfectly normal blood sugar, and three times with a slightly subnormal blood sugar. Among our last 17 cases coming to term, we have been making various blood chemical analyses, and once we observed a blood sugar which was slightly subnormal, 60 mg. This infant subsequently developed the whole train of symptoms which we associate with an insulin reaction in a juvenile patient, namely a sudden onset of sweating, pallor followed by cyanosis, twitchings, and convulsions. The blood sugar was found to have fallen to 9 mg. or one-tenth of the normal value. The symptoms were quickly relieved by the administration of glucose given by gavage. At the time we thought this was an example of spontaneous hypoglycemia, the first we had ever seen, but now we are afraid it was due to an overdose of insulin, for although the mother's blood sugar was perfectly normal, 70 mg., when she was on the operating table, her blood sugar too fell to subnormal levels and she had symptoms of hypoglycemia. Furthermore, the baby's blood sugar became stabilized on the third day. We doubt that this would have occurred with overproduction of endogenous insulin.

Asphyxia may be a serious problem in the neonatal period. It may result from the long labor which will occur in many of these pregnancies because of the large size of so many of the babies. Then too insulin itself is capable of producing cerebral edema, but, perhaps most important of all, because the acid base balance of a child of a diabetic mother is disturbed. Eastman⁵ has found that the carbon dioxide content of the blood of children born after relatively short labor was 48 volumes per cent, but this figure dropped to 40 volumes per cent with more difficult labor and anesthesia and to 38 volumes per cent in children who had severe asphyxia. In the infants of our series the average carbon dioxide combining power was 35 volumes per cent, the range being from 19 to 52. Earlier in this discussion we said that we did not think that the interoccurrence of acidosis during the early part of the third trimester was so harmful to the fetus. During labor it may be harmful, because if the alkali reserve of the mother's blood drops to less than 10 volumes per cent, a finding not unusual in diabetic coma, there will be associated with it a low oxygen content. This may have a serious effect upon the fetus, occurring when it is about to establish an independent existence. Even without acidosis asphyxia is a real problem and these babies particularly require plenty of oxygen, with proper aspiration, perhaps alpha lobeline or even a Drinker respirator.

Congenital diabetes⁶ is a rare occurrence. There are some eight, presumably authentic, cases reported in the literature, but the data are not very striking. Among the 170 infants represented in this series, one, a fatal case, had an elevation of blood sugar above normal; one subsequently developed diabetes at the age of four years.

The temporary unfavorable effects of pregnancy upon the course of diabetes are largely four: change in tolerance for carbohydrate; lower-

clinical manifestations of endocrine disturbance, particularly in the youthful diabetic. Examples are the failure of growth which amounts to actual dwarfism in some diabetic children, retarded maturity, and the long periods of amenorrhea in the adolescent.

Stillbirth is a third, perhaps, related failure. For years the obstetric diabetic literature has contained accounts of the frequency with which an overdeveloped, macerated fetus has been born to the diabetic mother. Here we wish to emphasize that this is not an unfailing characteristic of diabetes. The very fact that nearly half of all these pregnancies ended successfully prior to the general use of insulin shows without further comment that this is not the case. The cause of this overdevelopment, characteristic of so many of these pregnancies, has never been quite clear. It is natural that it should be attributed to overnutrition, to the elevation of blood sugar and blood fat, to the products of acidosis, and to hypoglycemia. Signs of these were lacking in our own series. Repeatedly it has been our experience, as well as that of others, that with a perfectly controlled case the fetus has died two, four, or six weeks prior to term. Yet the opposite situation with acidosis and even coma has occurred in this same apparently critical period, and patients have later been delivered of normal living children. Although it is granted that all of these factors need further investigation, still a new and interesting clew appears in the demonstration of an excess of serum prolactin (Smith and Smith). That prolactin is a substance capable of producing giantism has been demonstrated by Snyder¹ and Hoopes,² who have independently shown that injections of prolactin produce exactly the picture we see in diabetes, overdevelopment; death, and maceration of giant rat and rabbit fetuses. Thus, we believe that two definite forward steps have been made: first, when Dr. Titus decided to deliver these patients prematurely to anticipate the death of the fetus in utero, a procedure which was not entirely satisfactory, for we knew that not all of these patients were predestined to the development of this complication; second, when as appears now to be the case, we have a biologic test which indicates the cases in which the fetus is of the giant type described as characteristic of diabetes.

Congenital defects, hypoglycemia and asphyxia complicate the neonatal period. Congenital defects are doubtless beyond our therapeutic control. They are, we believe, related to a disease which is genetic in origin. It is an interesting association here to note that Priesel and Wagner³ have already reported the great frequency with which congenital anomalies occur in the true juvenile diabetic patient.

Hypoglycemia may be a dangerous complication in the neonatal period. It may result from a maternal overdose of insulin, or it may be due to an overproduction of fetal islet tissue. Hyperplasia of the fetal islands of Langerhans has been reported seven times⁴ in the literature, twice it has been known to occur with an elevation of blood sugar,

is to be delivered by normal labor, then she will require first of all constant attendance because she is a potential coma case. The carbohydrate intake should vary from 150 to 300 gm. with large quantities of fluid. If the patient is delivered by cesarean section, there is danger of the intercurrent of hypoglycemia, and since our experience with the infant whose blood sugar fell to 9 mg., we have been much happier when we have maintained a maternal blood sugar between 150 and 200 mg. than at that level which might be considered more ideally normal. After cesarean section the management of diabetes is that of any surgical case, specimens being tested every three hours and insulin prescribed according to the degree of reduction in the Benedict test.

Thus the diabetic during pregnancy is a candidate for coma in the first trimester, hypoglycemia in the second, acidosis, toxemia, and hypoglycemia in the third, and if she has normal labor, then the danger of coma is great and, perhaps, very serious indeed.

Another failure of many diabetic pregnancies is that of lactation. This has been observed in the diabetic animal as well as the diabetic woman.⁷ It is, perhaps, due to the lack of the specific lactogenic hormone of the pituitary gland. We think it is not related to calories, because it has occurred when the mother's diet contained between 2,500 and 3,500 calories and when we believe it to be adequate in all respects. Puerperal sepsis, contrary to our expectations, is rare in diabetes.

Genetic and eugenic problems arise. We believe that until the treatment of diabetes, even as good as it is today, improves, the diabetic should not have numerous pregnancies. Diabetes is a chronic, potentially incapacitating disease, predisposing the patient, even in youth, to a premature development of old age manifested by arteriosclerosis, retinal hemorrhages, cataracts, and diabetic neuritis. One must remember in treating these patients that the actual age is not the chronologic age, but as Dr. Joslin has pointed out, far more nearly the chronologic age plus the duration of diabetes.

Perhaps most important of all, we must answer the question, what are this child's chances of inheriting diabetes? We believe that we have presented evidence that the potentiality for developing diabetes is inherited insidiously through a simple Mendelian recessive gene,⁸ according to which theory it is necessary for both parents to contribute the genes for diabetes. A diabetic may arise from the union of two diabetics, a diabetic and an hereditary carrier, or two hereditary carriers. In calculating backward from the incidence of diabetes in the general population, we estimate that the incidence of carriers is very high, nearly 25 per cent of our entire population, so that in random mating the chances of a child of a diabetic eventually developing the disease are 1 in 4, and we must also remember that all of these children of diabetics are in turn hereditary carriers of diabetes.

ing of the renal threshold; predisposition to coma; and predisposition to hypoglycemia. The change in tolerance for carbohydrate, measured either by the insulin requirements or the elevation of blood sugar, on the average in this series was negligible. Individual cases, however, showed a wide variation, the greatest change generally occurring in the third trimester, when some patients who had required 50 units of insulin prior to pregnancy gave it up entirely until after delivery, and others required twice their former dose.

A low renal threshold generally occurred in the second trimester. The cause of this condition is not clear. It resembles the benign type of glycosuria associated with disturbances of the glands of internal secretion and is, perhaps, the result of changes in the endocrine glands, coincident with pregnancy.

Pregnancy favors the interoccurrence of acidosis because of the normally lowered alkali reserve, the depletion of glycogen, and the increased basal metabolic rate. The last two factors favor the interoccurrence of the opposite complication, hypoglycemia.

Thus the treatment of the diabetic during pregnancy will vary with problems of the individual patient and with the problems of each trimester. In the first trimester we will be concerned not only with the dietetic control of nausea and vomiting, the readjustment of the diabetic regime which this complication necessitates, but also with the accurate control of diabetes, which we believe prevents spontaneous abortion. If hourly feedings of carbohydrate food or parenteral glucose must be given, then we abandon our usual routine for insulin and administer it according to what Dr. Joslin likes to term "the emergency prescription," testing the urine every two, four, or six hours, giving 20 units of insulin if the Benedict test is red, 15 if orange, 10 if yellow, and 5 if yellow green. If nausea and vomiting do not complicate the first trimester, then there will be little need of readjusting the diabetic regime.

In the second trimester we are concerned with a low renal threshold and with the increased requirement for food. Here, to prevent hypoglycemia in the presence of glycosuria, we believe it is better to base changes in the dosage of insulin upon blood sugar analyses rather than upon urinalyses.

In the third trimester we are concerned over the possible development of acidosis. By this time the basal metabolism has become elevated to 20 per cent above normal, and the mother will require a definite increase in the number of calories. It has been estimated that the fetus metabolizes 50 gm. of glucose daily, and an allowance for this must be made in the mother's diet, so that we plan to give a minimum of 150 gm. of carbohydrate, 1 gm. of protein per kilogram of actual body weight, and 30 calories per kilogram of actual body weight.

Labor increases the complications of the third trimester, increases depletion of glycogen, and increases basal metabolic rate. If the patient

DIABETES IN PREGNANCY FROM THE OBSTETRIC POINT OF VIEW*

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INSULIN has made medical history. Insulin is making obstetric history. Before 1920 diabetes and pregnancy made a discouraging association. The only encouraging part of this association was its actual infrequency. It is well worth while to consider the reasons for this infrequency.

Before insulin the diabetic patients who developed the disease in the first and second decades of life had almost no chance of reaching maturity and motherhood, for the earlier in life the disease developed the more serious it was. In consequence, pregnancies in diabetics at that time occurred practically always in those cases in whom diabetes did not appear until the patient was in her twenties or thirties, and such cases of diabetes were recognized as being of the less severe type. When one considers that the average active fertile life of any woman is between the years of twenty and forty, and that before insulin practically none of the cases developing in the first decades survived to that age, one begins to see why the problem of diabetes and pregnancy before the discovery of insulin was numerically negligible.

Diabetes used to be considered a definite cause of sterility. Miscarriages among diabetics were recognized as probable sequelae of pregnancy. Furthermore, pregnancies occurring in these diabetics were prone to result in dead babies before viability or overdeveloped, macerated babies after eight months; it was very unusual for a case to be delivered of a living child, and it was only in the milder diabetics that pregnancy was considered a worth-while venture. Because of the reasons just enumerated, diabetics who did become pregnant were very often advised to be aborted.

The foregoing shows why pregnancy complicating diabetes was not a real problem before insulin was discovered.

What insulin has done for the general diabetic insulin is now doing for the pregnant diabetic. It has increased the fertility in those in whom diabetes occurs between the years of twenty and forty and holds the disease in check. It has saved the lives of children developing diabetes before or during the teens so that they have lived to maturity and maternity.

With the very appreciable increase in the number of diabetics who may become pregnant for the above reasons, the problem of the

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In conclusion, we believe (1) that the incidence of spontaneous abortion may be reduced by more accurate control of diabetes; (2) that toxemia and eclampsia occur with great frequency, particularly in the youthful type of diabetes; (3) that related to these complications is the common complication of the diabetic pregnancy, a giant fetus; (4) that deaths in the neonatal period are largely due to congenital defects which are beyond our therapeutic control, to hypoglycemia which can be corrected, and to asphyxia to which the infant of the diabetic patient is undoubtedly more liable than that of the non-diabetic, because of the greater danger of toxemic and diabetic acidosis; (5) that the treatment of the diabetic patient during pregnancy must be individualized; (6) that the diabetic woman should not have numerous pregnancies, because diabetes carries with it a morbidity hazard, but most important of all, that the potentiality of developing the disease is inherited.

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The abnormal proliferation of the endometrium as a result of a persistent ripe follicle without ovulation has been named "glandular cystic hyperplasia." This condition is attended with necrobiotic areas occurring in the thick mucosa and subsequent irregular and protracted bleeding. It is a disturbance in the genital cycle, marked by the absence of ovulation corpus luteum phase and a true menstrual process.

Wherever it was possible to examine the ovaries he confirmed the presence of ripe follicles and the absence of a corpus luteum. The cystic atretic follicles do not exert this influence on the endometrium.

The condition occurs most commonly at about the age of 40 years. Diagnosis is established by means of curettage. Pelvic examination for the determination of the size and condition of the ovaries is an essential factor.

Treatment is causal and general. Hormone therapy is indicated in the hypoplastic conditions and in menorrhagia without palpable lesions.

In atypical bleeding from a myomatous uterus myomectomy often is indicated or total hysterectomy may be required. X-ray sterilization was resorted to in a few instances. In chronic metritis radium is the treatment of choice.

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carrying with it, of course, unnecessary morbidity to the mother; and the mother has the same right to demand a living child, if diabetes does not kill the child before viability.

Before going any further in the discussion of diabetes and pregnancy, I want to make it perfectly clear that up to the point of deciding when and how to deliver pregnant patients, the problem is a medical problem. No one should entertain the handling of these serious diabetics who is not thoroughly conversant with diabetes. The proper handling of these cases from start to finish means intelligent cooperation between the diabetic specialist and the obstetrician, and any obstetrician who is courageous enough or ignorant enough to assume the responsibility of handling these cases during pregnancy and delivery, either normal or operative, without having in attendance during the entire labor the physician expertly trained in the care of diabetes, is assuming a burden which he has no right to assume, and a burden which if assumed may well lead to the death of his patient.

All that I have to say about this subject of diabetes and pregnancy and its obstetric management is based upon what I have learned and deduced from our study of forty-three cases. Far be it from me to say that my conclusions are the only right conclusions; that my suggestions on the handling of these cases are the only right suggestions.

I shall concisely review certain of these cases, showing the successes, the failures, the pitfalls, and hoping to point out my reasons for the conclusions which have seemed intelligent and conservative rather than unnecessarily radical. No one really knows anything about this problem. With more experience the present point of view may not be at all tenable, and I realize most of all that all the babies of these diabetic mothers at the present state of our knowledge and the present handling of these patients cannot be guaranteed life.

In this series of 43 cases, one occurred before 1920. In the last two years there have been 16.

There were: 21 primiparas, 22 multiparas, 12 normal deliveries with living children, 14 cesarean sections, 5 cases of breech, 10 miscarriages or interruptions of pregnancy in the first three months, 6 hysterotomies, 2 deliveries at seven months, 4 inductions by rupturing the membranes when induction was practicable at eight and one-half months plus. 1 case of twins, 3 macerated babies, and 5 "insulin mothers" (patients who before insulin would not be alive).

There were the following complications: 2 cases of hydramnios, 3 cases of coma developing during pregnancy, 7 toxemias, 1 case of pyelitis during pregnancy, and 1 gallbladder attack during pregnancy.

Not a mother was lost.

So we see in this series that from the standpoint of the mothers, mortality and morbidity are well controlled by insulin.

obstetric management of these cases must be given very serious thought and consideration. It is a real problem and one that more and more is going to demand definite unity of obstetric opinion. The whole problem is so young that no one really knows anything about it. There have not been enough cases upon which to base obstetric laws as to their management, so that all we say here are our own views, and have gradually evolved as case after case has taught a new lesson. We can assert from our experience that insulin makes pregnancy safe for the mother, but it does not insure fetal life to viability or survival after delivery.

As in other conditions complicating pregnancy, when no one rule as to their handling can intelligently be laid down, no one method of treatment can hope to encompass the proper treatment for all diabetics. As it is extremely unintelligent to say that all nephritics should be delivered in one fashion or that all cardiaes should be delivered in one fashion, so it is also unintelligent to say that all diabetics should likewise be delivered and handled in one fashion. Each diabetic must be individualized. The mild one certainly does not need the extreme care during pregnancy nor at term that the severe diabetic should receive. It is not intelligent to infer that the mild diabetic who has one or two children living, whose diabetes is absolutely under control, should be delivered in any but the natural manner. It is intelligent to assume that the severe diabetic, one who developed the disease as a child, who is living and pregnant because of insulin, is a very different problem and one that deserves much more thought and attention. As I have said, insulin saves the lives of these diabetics who become pregnant. It has not yet saved all the babies.

Diabetics of a severe type are advised against any added load. If they have infected teeth, these are removed. If they have a skin infection, this is watched very carefully. If they develop pneumonia, their diabetes may at once become almost uncontrollable. Is it not logical to infer that the drain of pregnancy on diabetics of this type of severity may not make subsequent pregnancies inadvisable, thus increasing the value of each pregnancy, and if this is so, is not each baby of much greater value than the individual baby in any normal pregnancy? The obstetric problem really is a reduction of the mortality of these babies. All study, all effort, all methods of delivery should attempt to provide a living child for each individual diabetic pregnancy.

We do not really know what the effect of pregnancy in after-years is on these serious diabetic mothers. Enough time has not yet elapsed for any definite conclusions upon this subject. At the present time we feel that in this type of case each individual baby, because it may seem wise that this mother should have no more babies, has a right to demand that it be delivered by that method which will guarantee, as far as is humanly and obstetrically possible, its safe arrival, without

In this analysis, there are certain cases that I call key cases, that I would like somewhat specifically to point out.

CASE 1.—R. This is the only diabetic whom I took care of before the discovery of insulin, with a living child. This case is referred to merely to bring out the time element.

CASE 2.—Mrs. G., thirty-nine years old, who had had 13 pregnancies, with no living children, entered the hospital in coma at approximately six months. This is the first case in Dr. Joslin's experience in which the baby survived intrauterine life in spite of diabetic coma in the mother. Patient was delivered at eight and one-half months by cesarean section, under spinal anesthesia. This case stimulated Dr. Joslin's interest in the subject of pregnancy in diabetes, because it showed him that insulin could prevent an intrauterine death from diabetic coma, and all that has been done on diabetic patients since then has been done entirely because of Dr. Joslin's enthusiasm.

CASE 3.—Mrs. H., thirty-five years old, had had 2 previous babies, the first still-born at term, the second stillborn at seven months. This child died at approximately eight and one-half months. The delivery was normal. The baby was macerated. This was an obstetric failure in spite of insulin, a failure that delivery after eight months assuredly would have prevented.

CASE 4.—Mrs. G., twenty-one years old, had had diabetes since she was eight years old. Patient went into severe coma at the onset of labor, at which time the baby was alive. After a labor of twelve hours the baby was born with beginning maceration. The coma was deep and the patient was given a tremendous number of units of insulin. This case illustrates how tragic it is to have a baby alive now and dead in ten minutes in an insulin mother whose number of pregnancies, in the present stage of our knowledge, must be limited.

CASE 5.—Mrs. C., a primipara, nineteen years old, started in labor, with a breech, and was delivered by cesarean section. The operation was done because she was a diabetic who developed diabetes as a child, and it was done to avoid any possible fetal injury. The interesting thing about this particular patient is that she had a child that weighed seven pounds, five ounces, when, to the best of calculations, she was well under eight months.

CASE 6.—Mrs. P., a primipara, twenty-nine years old. When about six months pregnant she gained much too much weight, developed a great deal of edema and was in the hospital with a blood pressure of 130 plus and some albumin. Her uterus was big with a large amount of fluid and a good-sized baby. Because of the size of the baby and the toxemia she was delivered while under eight months, by cesarean section, of a baby weighing ten and one-half pounds, and the baby is alive and well today. This case, as well as the previous case, illustrates the size to which some of these diabetic babies develop, also the problem of toxemia that is seen not at all infrequently associated with diabetes in pregnancy.

My experience with the fourth case was so tragic, I felt so badly about having lost a baby which died under our observation that the general rule was laid down to deliver all these insulin mothers and sick diabetics by cesarean section as soon as it was felt that the baby was viable. Our experience with Cases 5 and 6 accentuated in our minds the tendency toward overdevelopment of these babies in certain diabetics, and made us wonder whether or not certain of these cases did

In this series there were nine babies who did not survive, in pregnancies that lasted seven months or more.

From this we see that the fetal death rate, from all causes, is still tremendously high. Let us analyze these fetal deaths, and see which ones might have been prevented.

First, the patient at seven months with hydramnios, whose baby died a few hours after birth of atelectasis and hemorrhagic disease. We do not know the cause of acute hydramnios. Some day this may be prevented. We can hardly be blamed for the death of a baby at seven months of atelectasis and hemorrhagic disease. Each problem cannot begin until the infant has reached a normal viable state, and the nearer eight months or, better still, the farther beyond eight months interference is considered advisable, the better the chance on the baby.

Second, the death of a twin at eight months, who lived twenty-four hours and died of cerebral hemorrhage. This was the second of the twins, the bigger of the two. It was a simple double footling extraction, and it is very difficult to understand how the delivery caused the cerebral hemorrhage.

Third, the macerated baby at term who weighed 6 pounds, 7 ounces, and died in utero at seven months plus is another of the unavoidable disasters that pregnant diabetics must face. This patient, although a toxemic, had not advanced sufficiently to hope for the infant's surviving if the pregnancy were terminated, and the toxemia itself was not clinically severe enough to warrant interruption. These possibilities always exist. They are the unavoidable chances that diabetics must take, and the possibilities must always be told these patients when they embark on the stormy sea of a diabetic pregnancy.

Fourth, a baby dying at seven months of prematurity, the mother in labor, and ill with pneumonia. This was a breech, which lived just a few hours and weighed five pounds, twelve ounces.

Fifth and sixth, two cases of intrauterine death after viability which resulted in macerated babies. These two babies, had they been delivered after viability, might have been saved.

Finally, of the cesarean babies that did not survive, there were three, one that was delivered at eight and one-half months, who died of congenital heart, revealed at autopsy; one delivered at seven and one-fourth months, with patient in acidotic condition, beginning coma, starting labor with a living child, who weighed 7 pounds, 6 ounces, and died in ten hours of prematurity (her previous pregnancy had resulted in a dead baby at seven months); one delivered at eight months plus, who weighed 8 pounds, 1 ounce, the autopsy showing "prematurity."

Fetal deaths that occur after eight months from coma or from the fickleness of diabetes are fetal deaths that may be obviated by delivery while the child is alive. This is really the obstetric problem of the management of these cases, and if 6+ per cent of the babies in this particular series of possible living children are lost from maceration when they might well have been saved by delivery after viability, the problem is still one worthy of further consideration and study. The method of delivering these patients may well be questioned. My feeling is that in the "insulin mother," who ought to have no more than one or possibly two pregnancies, the child takes on so much added value that cesarean section is not a radical performance.

it involves no possible complications and, so far as I know, no one of the patients upon whom I have performed it has since become pregnant.

No review of this subject is complete without saying something about these babies after birth. It is not nearly enough to deliver them alive. If one feels that the case may be considered successfully treated when the child is delivered living, one does not understand the problem of these newborns. Is it not fair to wonder if there is not something that we at present know nothing about inherent in these diabetic children that causes the death of one weighing 8 pounds, 1 ounce, and another weighing 7 pounds, 6 ounces, at birth? We do not expect to lose from just prematurity a child that weighs 8 pounds, 1 ounce, and another that weighs 7 pounds, 6 ounces, whose autopsies show no gross pathology. The strange reactions of some of these babies for forty-eight hours after delivery have led us to know that it takes these little infants quite some time to adjust themselves to independent living. It seems as though their metabolic reactions were all wrong, possibly because of the immediate withdrawal of the influence of the insulin that their mothers have been taking. One of our babies had convulsions, and its blood sugar was the lowest that Dr. White has ever seen. Another of our babies developed general anasarca, pitting edema appeared twenty-four hours after birth, and there was edema of the lungs. There was no blood sugar done on this child at the time, so we do not know what its blood sugar was, but twenty-four hours later it had overcome whatever was wrong and thereafter appeared and behaved like a normal infant. All of these babies must be under very expert care from the moment of delivery. Our babies are under the care of special nurses for at least forty-eight hours. Once the readjustment has satisfactorily taken place between the entirely dependent life before birth and the comparatively independent life after birth these babies have done well; but inasmuch as one of the aims of diabetes and pregnancy should be to insure living children to each diabetic mother, the care of these infants as soon as they are born must be as expertly handled as the care of the diabetic mothers up to labor and delivery.

Now, in conclusion, let me emphasize: That insulin is increasing every day the number of possible pregnancies in diabetics. That these diabetics who become pregnant must be under the most efficient medical care. That no obstetrician should think for one minute of handling these cases alone. That insulin makes pregnancy safe for the mothers. That present knowledge cannot guarantee living children. That the method of delivery must be individualized. That the baby is so very important in the severe diabetics and in the "insulin mothers" that, to avoid intrauterine death, the safest method is cesarean section when the baby seems quite big enough.

not superincubate their babies and develop them prematurely so that they became overripe children before nature took the initiative and started labor, with the frequent result of macerated stillbirths. Consequently, since that time cesarean sections have been done on this particular type of diabetic. All the babies are living and well with the exception of two, one that weighed 7 pounds, 6 ounces, whose autopsy showed prematurity and atelectasis, and one that weighed 8 pounds, 1 ounce, whose autopsy showed only "prematurity."

If one contemplates the delivery of these babies before labor starts, one sometimes is in a quandary as to the exact duration of pregnancy because of the absence of specific catamenial history. A few of these cases were extremely irregular, being unwell only once in six or eight weeks. One of our patients had the peculiar habit of being very irregular in the summer, and as the cold weather approached her periods appeared at a normal interval. If one feels that delivery is warranted to avoid intrauterine death and maceration after viability, one surely does not want to deliver these babies too soon. One wants to be as sure as one can be that the child is viable, that the child is big enough to survive. In the case of the overdeveloped infant, this is not a very difficult problem, but all of these diabetic babies are not overdeveloped. Some of them are small. The use of the x-ray at intervals after the patient has reached what we think is seven months may ultimately prove to be a very helpful procedure. Our experience to date with x-raying these babies to determine their size has not been particularly satisfactory, but that is no reason why the x-ray should not be used, because I am sure that its establishment as a piece of routine will ultimately be of inestimable value.

Now, just a word about the use of spinal anesthesia in these cases. The first patient upon whom we did a cesarean section was Mrs. G., and spinal anesthesia was chosen because it had been the anesthesia used in a good many of Dr. Joslin's abdominal cases. It was so satisfactory from every point of view that it has since been the routine anesthetic. The relaxation was perfect. There was no intestinal straining. There were no unpleasant sequelae following its use. The operation, because of the perfect relaxation and the absence of intestinal straining, has been done with the greatest amount of ease and celerity; and it seems that any anesthetic which makes the operation simpler, consequently consuming much less time, and avoiding the need of walling off straining intestines, is an anesthetic which has a great deal to be said for itself. I have been so impressed with its use that I have used it thirty-six times in normal cases of cesarean section and hysterotomies.

The operation of sterilization in all but one case has been done in the very simple manner described by Bishop. It is an operation which I think deserves more widespread acceptance. It takes almost no time.

PRESENT ETIOLOGIC THEORIES

The causes given by various authorities are very many and varied. For brevity and clarity they can all be accommodated in the following classification:

I. Causes that operate by delaying the passage of the ovum so that the active agent of nidation, the plasmodial trophoblast, is developed before the zygote reaches the uterine cavity.

A. Intratubal partial obstruction: concurrent salpingitis, postinflammatory agglutination of tubal folds, and intratubal tumors.

B. Extratubal partial obstruction: Compression, torsion or distortion of tube by tumors, peritubal inflammation, or adhesions.

C. Lengthening or kinking of the tube.

D. External migration of ovum, the wandering of the fertilized ovum to the tubal ostium of the opposite side.

II. Entrapping of the zygote in false passages so that it is forced to imbed at the place where its progress to the uterus is halted.

A. Tubal anomalies: Diverticula, accessory tubes, accessory ostia.

B. Labyrinthine branches from the true tubal lumen resulting from adhesions of tubal folds after the subsiding of gonorrheal salpingitis.

CONSIDERATION OF THESE THEORIES

In 7 of the 29 cases above mentioned, there was definite evidence of previous inflammation of the tube. In the remaining 22 cases, none of the enumerated etiologic factors could be demonstrated at all. It was this that led to our undertaking a definite search for a common cause.

The occurrence of gestation in an anomalous tube is very rare and can be dismissed from consideration as an important cause.

External migration of the ovum is only hypothetical except in those cases where the tube on the side of the follicular rupture is absent or completely occluded, and therefore can be only an unimportant factor.

Intratubal and extratubal tumors and adhesions as potent factors were not demonstrable in any of our cases. The same can be said of kinking or stretching of the tube.

This leaves for active consideration false passages in the tubal lumen created by agglutinated tubal folds. Hahn² stated that gonorrhea is the commonest cause of extrauterine pregnancy, since this type of pregnancy is commoner in large towns where gonorrhea is more frequent and where both these conditions are increasing in frequency. Falk,^{3,4} noted the same for this country and stated that ectopic gestation was more frequent in Harlem where the incidence of gonorrhea is notoriously higher than in certain Quaker settlements in Pennsylvania where both social diseases and ectopic pregnancies are rare. Yet it could account for only seven of our cases or 23 per cent, leaving 77 per cent unaccounted for. It was plain that our etiologic factor could not be found in those enumerated. In addition, none of these causes could account for primary abdominal pregnancy.

THE ENDOMETRIAL THEORY OF ECTOPIC PREGNANCY*

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IN A PREVIOUS communication to this JOURNAL,¹ we referred to the project which forms the substance of this paper.

Six years ago while doing research work on tubal pregnancy it occurred to one of us (J. M. F.) that rarely could he satisfy himself that sufficient gynecologic pathology existed to justify the selection of an etiologic factor. It was found by him that patches of decidual tissue frequently occurred at the site of implantation of the gestation in the tube. In some specimens the decidual tissue was present only in shreds, in others in considerable amount. Out of this grew the idea that this was incidental and not accidental. In 1933, 29 patients with tubal pregnancy were operated upon at the Jewish Hospital of Brooklyn. In all of these patients the affected tube was removed. A routine section was taken by the pathologist from each specimen for histologic examination. In the pathologist's report the presence of the decidual tissue was sometimes noted, but more often not, since the search was mainly for the important diagnostic element, the chorionic villi, and the single section studied was one taken at random. Frankel went over these casual histologic slides more carefully and found that in 18 cases or 62 per cent he was able to find more or less well-defined decidual tissue. This frequency made the suspicion stronger that there might be a possible physiologic relationship between the decidual tissue and the ectopic gestation.

In 1934 we set out to find whether any such relationship existed and as a result of our research, we believe we can now set forth the following as hypotheses:

1. The etiologic factor in the production of extrauterine pregnancy is the prior existence of endometrial tissue in an ectopic site.
2. The fertilized ovum by positive chemotactic attraction migrates to the ectopic endometrial tissue and implants there.
3. The ultimate fate of the pregnancy depends on (a) the amount of ectopic endometrial tissue present, and (b) the depth of penetration of the ovum into the structure in which the ectopic endometrium is harbored.
4. Ectopic pregnancy is always primary and never becomes secondary; when it is extruded from the fallopian tube following rupture of that viscus or abortion through the fimbrial end, it does not continue its development.

*Read before the Section on Gynecology and Obstetrics of the New York Academy of Medicine, December 17, 1935.

was a piece of tissue consisting of tubular glands surrounded by a cytogenic stroma. That was found in the isthmic portion and ampulla portion of the tube. The infundibular section of the tube differs only in that the tissue in the lumen was in three small shreds, one of which was partly covered by columnar epithelium. These structures were readily identified with endometrium.

CASE 2 (142).—Both tubes removed with a fibromyomatous uterus. Both tubes grossly and microscopically normal. In the lumen of one tube at the ampulla was found a shred of endometrial tissue wider than in the previous case lying free.

CASE 3 (95).—Both tubes were removed with a fibromyomatous uterus and were grossly normal. One tube was microscopically normal, but the other had imbedded in the muscular wall of the tube in its ampullar part groups of tubal glands each surrounded by cytogenic stroma, each group more or less separated from the others

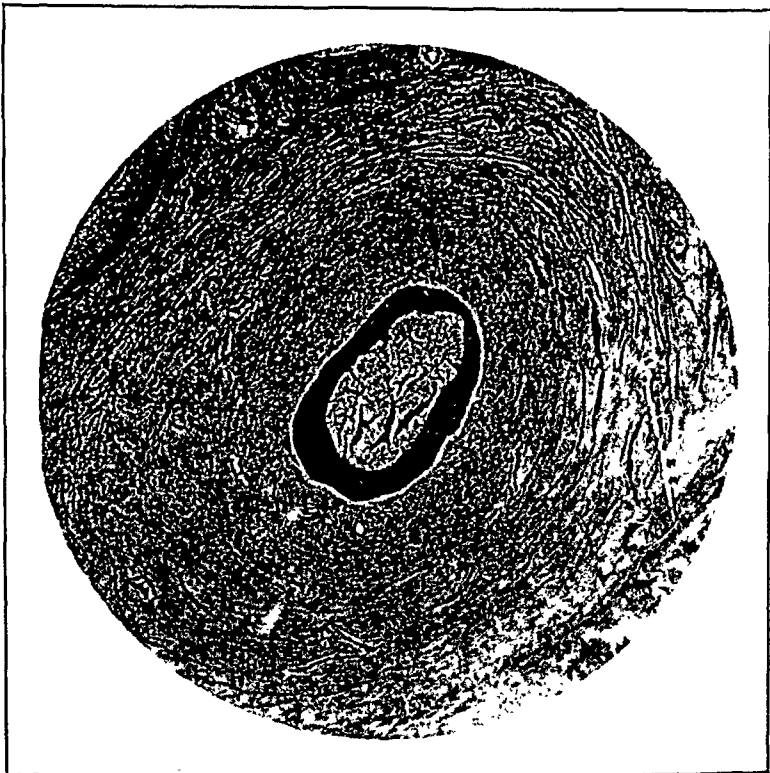


Fig. 2.—Case 142. Endometrial tissue lying in lumen of uterine end of tube.

by muscle tissue. This was also definite endometrial tissue and was in the nonsecretory phase. It was absent from infundibular and isthmic sections of the tube. As the ampullar joined the infundibular, the endometrial tissue was more abundant and lay close to the serous surface of the tube, while toward the isthmus the endometrium became scant and lay more deeply in the muscle.

CASE 4 (158).—Tube was removed for ectopic pregnancy. It was markedly enlarged, being 3 cm. in diameter. The surface was smooth and bluish pink. On section it was found to be distended with a blood clot in the center of which was a small smooth lined cavity. Microscopically one wall of the tube contained the blood clot in which were chorionic villi. The tubal lumen narrowed and compressed against the opposite wall, the folds being rendered more shallow and flattened. Decidual tissue was found at the periphery of the blood clot. In that portion of the decidual tissue lying on the muscle toward the periphery of the tube were found several endometrial glands. The decidual cells were individually recognizable only in spots,

PRESENTATION OF CASES

In 1934, we began to examine carefully all tubes removed at operation for whatever cause. Histologic study was made of sections through the isthmus, the ampulla, and the infundibulum of each tube. Tubes the seat of ectopic gestation were sectioned serially from end to end. To date we have examined a total of 204 cases. In 94 cases both tubes were removed at the operation, while in 110 cases only one tube was excised. This latter group includes 16 tubal gestations.

In Case 95, we found conclusively in one tube an endometrial patch in the muscular portion of the tubal wall. Cases 109 and 142, the

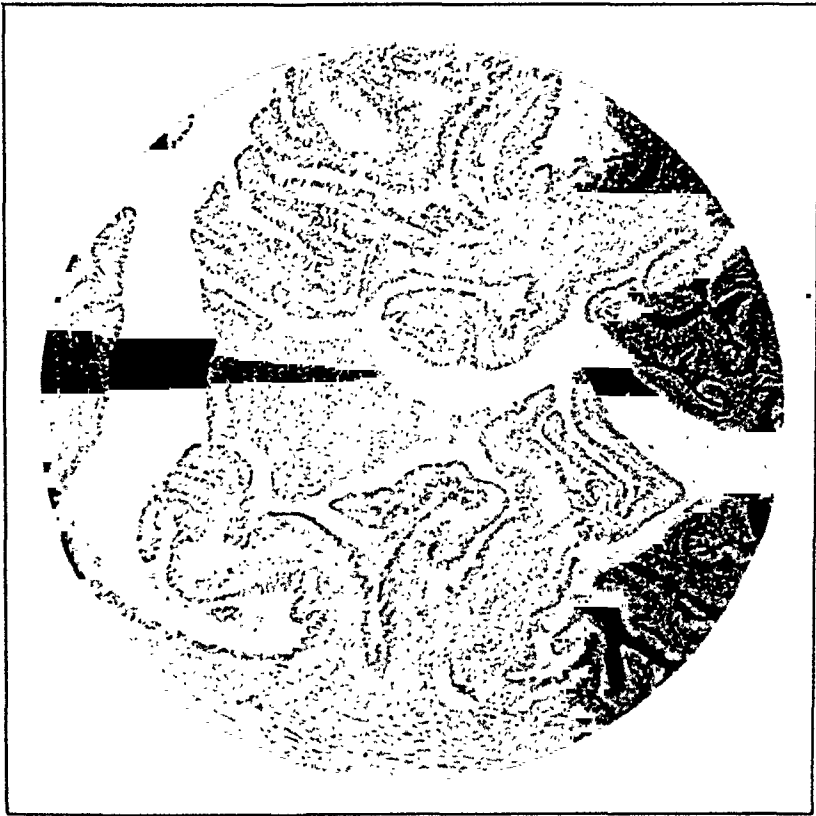


FIG. 1.—Case 109. Endometrial tissue lying in lumen of tube.

former consisting of only one tube while the latter had two tubes, only one of which contained peculiar structures, we found shreds of endometrial tissue lying free in the lumina of the tubes. In Case 158 there was a tubal gestation that contained in its decidual tissue demonstrable endometrial glands. In the 16 pregnant tubes well-defined decidual tissue was present at the implantation site, in 14 cases, and there only, while two cases were so distended by old clotted blood that, aside from the surrounding muscular wall and the contained blood clot containing a few ghosts of villi, no other structures could be made out.

The case reports are given in detail.

CASE 1 (109).—One tube removed with the uterus for fibromyomas uteri. The tubes were grossly and microscopically normal except that lying free in the lumen

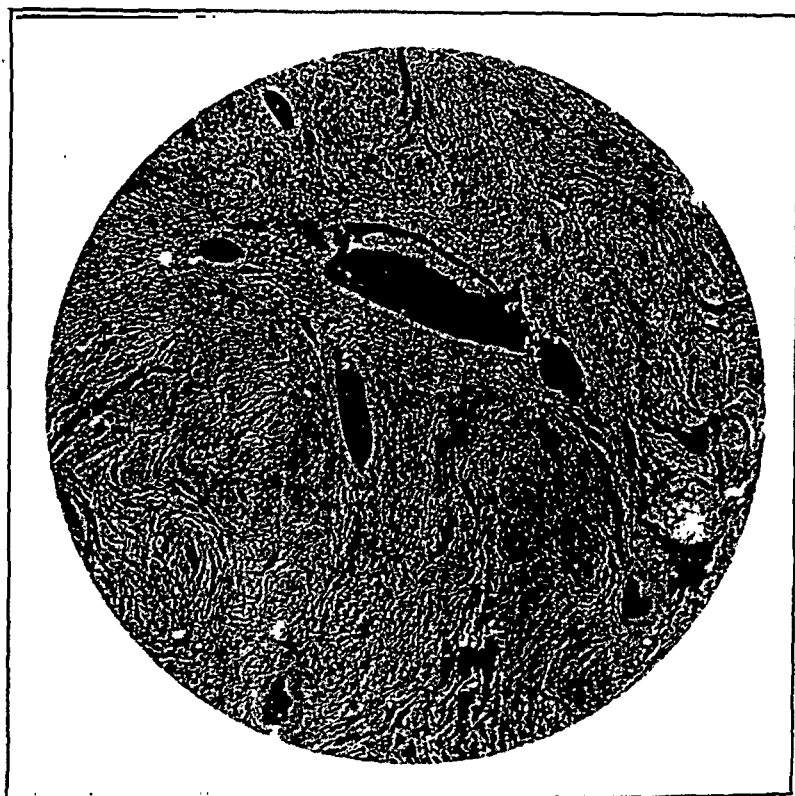


Fig. 5.—Case 95. Endometrial implant in wall of tube, abdominal end.

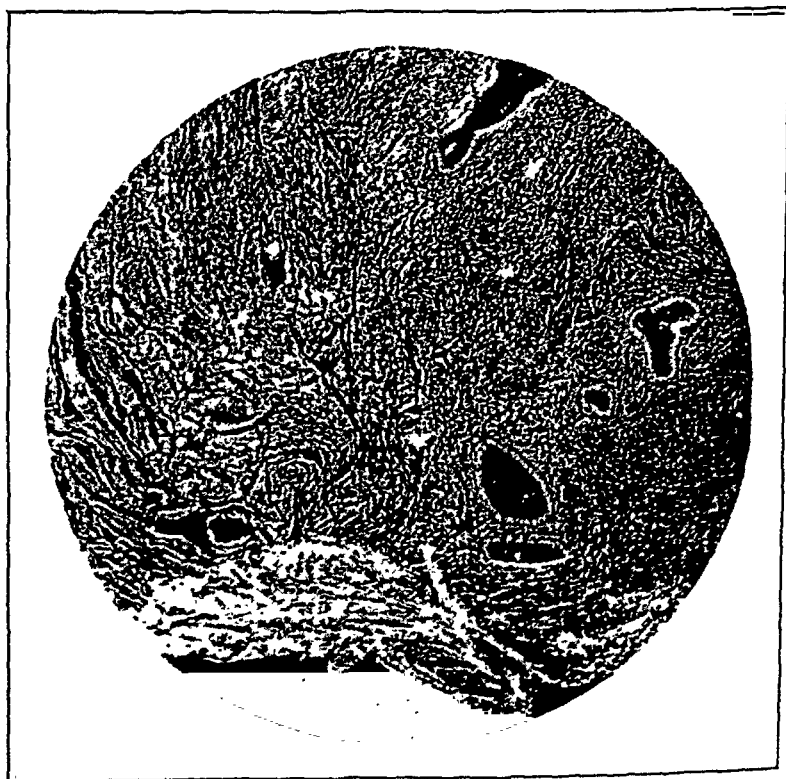


Fig. 6.—Case 95. Endometrial implant in wall of tube-isthmic part, glands are numerous, lie close to serous surface.



Fig. 3.—Case 142. Endometrial tissue lying in lumen of isthmie portion of tube.



Fig. 4.—Case 142. Endometrial tissue lying in lumen of ampulla end of tube.

2. Endometrial tissue was found imbedded in the tubal wall and its proximity to the serous surface of the tube suggests that it was a serous surface implantation originally.

3. Endometrial glands were found in the decidua of an ectopic pregnancy, definitely identifying it as decidual change of endometrial tissue, not as a possible decidual reaction of tubal wall elements. Time does not permit, nor is it necessary here, to quote Sampson's^{5, 6} linking of the above phenomena into a chain of evidence to prove how endometrial implants occur and that their origin is from detached shreds of endometrial tissue, or Jacobson's⁷⁻¹⁰ work, showing that such fragments are able to implant and grow in other locations after their detachment.

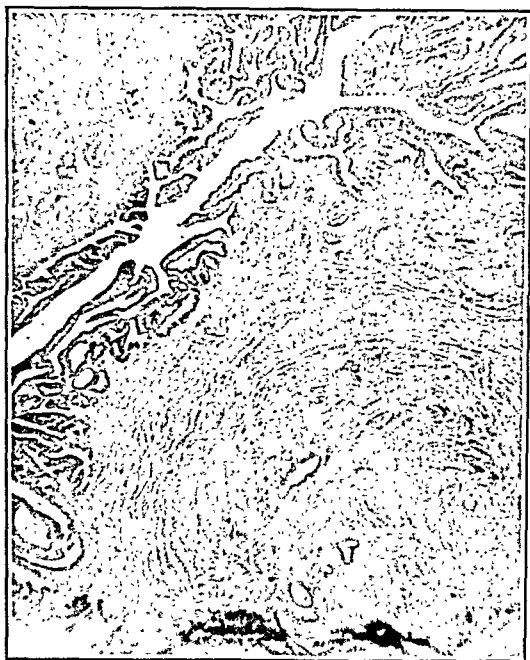


Fig. 9.



Fig. 10.

Fig. 9.—Low power view of Fig. 6.

Fig. 10.—Low power view of Fig. 7.

4. Decidual tissue was not found in two cases of the series of 16 tubal pregnancies because of the wide destruction of the tissues by hemorrhage, but was found in the other 14 cases where the anatomy was not disrupted.

Endometrium is tissue with a specialized function, but its structure is simple and less differentiated than other body tissues. Novak says that the glands are simple tubules and that the stroma is simple labile embryonic connective tissue. Its lack of differentiation enables it to assume readily the wide range of changes it is forced to go through in response to hormonal influences and to regenerate speedily after most extensive denudation, and also accounts for its ability to form endometrial implants.

the greater portion of them being converted into the hyaline-like band of Nita-busch's fibrin layer. Other sections through this specimen showed the breaking through of the fetal elements into the tubal wall where the decidual layer was deficient.

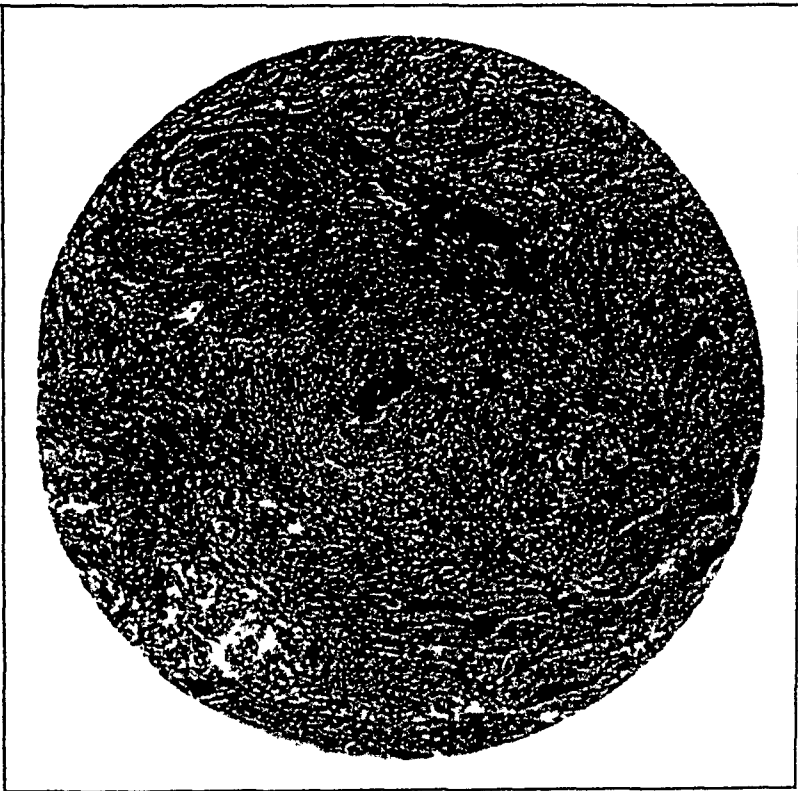


Fig. 7.—Case 95. Endometrial implant in wall of tube-uterine end; glands grow fewer as the tissue is followed and lie farther away from serous surface.



Fig. 8.—Case 95. Endometrial implant in wall of tube; low power view of Fig. 5.

Thus, logically, we can trace the steps that led us to our conclusions:

1. Endometrial tissue was found lying free in the tubal lumen and could have originated only in the uterine cavity.

favorable ones. This, we believe, is the decisive element in the implantation of the fertilized ovum. It appears to us a logical assumption as reasonable as the assumption that the spermatozoon is attracted to the ovum. It has been shown that the plasmodial trophoblast imparts to the zygote a certain degree of motility.

For these latter assumptions we have no definite proof, but we believe them to be correct; they become convictions on consideration of the evidence we have been able to accumulate.

CONSIDERATION OF THE LITERATURE

The finding of decidual tissue in ectopic locations is not new. As far back as 1897 Webster¹¹ described decidual tissue in tubal pregnancy. In 1904¹² he reported a case of ovarian pregnancy and mentioned the finding of decidua-like cells on the surface of the ovary and that Schmorl had observed the same. He found these decidua-like cells in uterine pregnancy in other sites of the pelvic peritoneum—the places that Cullen taught us to look for adenomyosis and Sampson for endometriomas. But he believed that the tube could and did produce a decidual reaction when pregnancy occurred (even intra-uterum) because genetically it arose from müllerian tissue like the uterus.

In 1931 Weiss¹³ reported finding endometrium in five fallopian tubes, one a pre-gravid stage, premenstrual in another and quoted cases reported by others, 2 by Schridde and Schonholz, one by Hohnes (in which the endometrium was found in the intramural part of the tube) one by Schwarz and Crossen, one by Schindler, one by Szamek (endometrium in the right and left tubes), one by R. Meyer demonstrating functioning endometrium in the tube.

Osiakina and Schmatok¹⁴ in 1933 found a decidual reaction in the tube in 21 per cent of a series of 21 tubal pregnancies independent of the localization of the implanted ovum.

Frank¹⁵ says that decidual formation in the tube is imperfect and is limited to a few tubal folds. Kermauner¹⁶ found decidua in 15 per cent of cases. Litzenberg¹⁷ says that though decidual reaction can sometimes be found in pregnant tubes, it is limited to only a few cells and a true decidual basalis is never present. Like many others he believes that it is the tubal mucosa that undergoes the decidual change due to the presence of the chorionic villi. With this view, however, we cannot agree for all evidence is against it. But the paucity of decidual tissue to be found we have to admit. But this is due to the small size of the primary endometrial implants. If the endometrial tissue were sufficiently large, all cases of ectopic pregnancy would go on developing at least until the fetus had reached full development, and no tubal ruptures would ever occur. There is universal agreement that the decidua has a two-fold action, affording on one hand a nearly perfect bed for the embryo, on the other preventing, by the formation of the fibrin layer of Nitabusch, wild ungoverned invasion by the chorionic villi. No other tissue can resist this penetration and continue to harbor the zygote. In ectopic pregnancy it is the scantiness of the barrier that causes the tubal rupture and the death of the embryo, because as soon as the villi invade extradecidual tissue, coagulation of the blood in the sinuses occurs and the embryo has committed suicide. This brings up the question of secondary abdominal pregnancy.

SECONDARY ABDOMINAL PREGNANCY

It has been quoted repeatedly in textbooks and elsewhere as indubitable, that a tubal pregnancy may lose its position in the tube and

The endometrium offers the only possible nidus for the embryo and exists only for that purpose. This implies the existence of a bond, an affinity and a positive chemotactic attraction on the part of the mobile

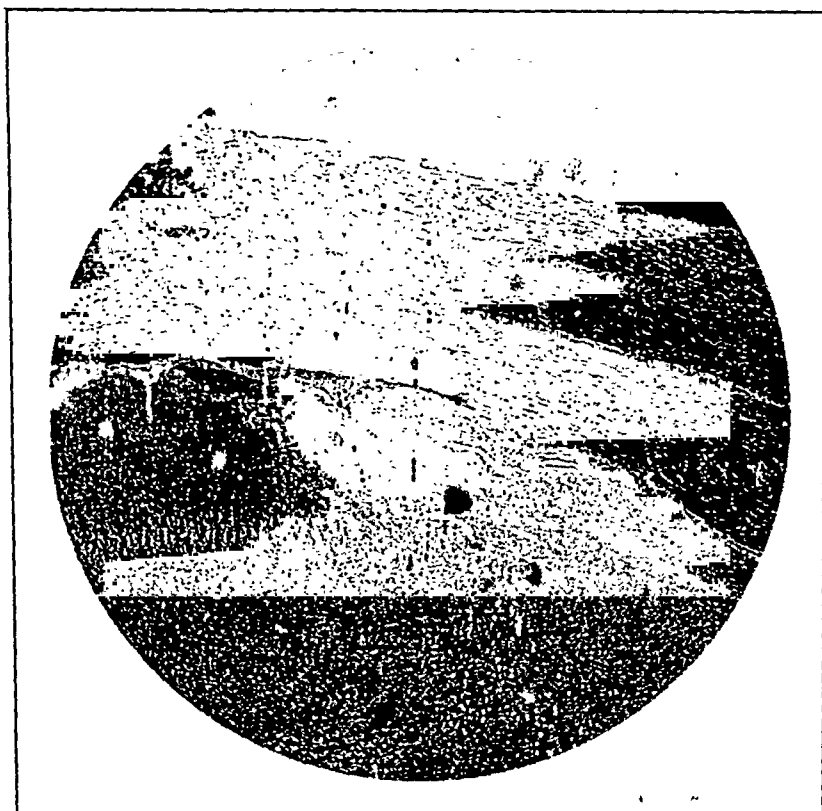


Fig. 11.—Decidual tissue, containing endometrial glands, in wall of tube the site of ectopic gestation.

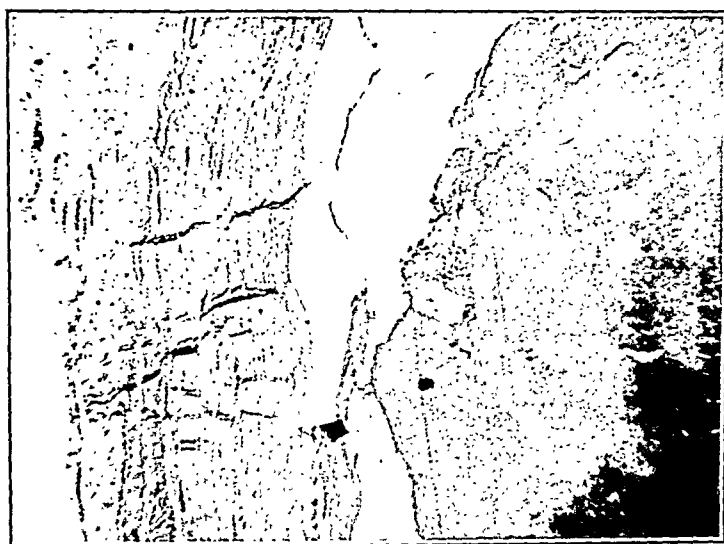


Fig. 12.—Low power view of Fig. 11.

zygote which at this stage behaves like any of the protozoa and possesses the general properties common to all protoplasm, including definite reaction to stimuli, repulsion from unfavorable stimuli, attraction to

2. The fate of the gestation depends upon the amount of endometrial tissue present to undergo the decidual reaction and upon the depth of penetration of the ovum beyond the borders of this decidua.

3. All ectopic pregnancies are primary.

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A HISTOLOGIC METHOD FOR THE EARLY DIAGNOSIS OF PREGNANCY

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INTRODUCTION

IN A PREVIOUS article (Smith and Brunner, 1934) we described a modification of the typical structure of the human vaginal epithelium which, we thought, might be of practical importance in the early diagnosis of pregnancy. Subsequently, we have examined this question with the advantage of much additional material. The results of this study are set forth in the present paper.

In order to recognize any peculiarities of the vaginal epithelium associated with pregnancy, one must be familiar with the normal structure during the menstrual cycle. Also, one must be able to recognize the common pathologic modifications of the vaginal mucosa, modifications which, in some cases, make this method of diagnosis inapplicable. Since this background is supplied by our previous paper, brief descriptions will suffice here.

MATERIAL AND METHODS

All the material considered in the present paper was obtained by the method of biopsy. Very small pieces, seldom exceeding 3 mm. in diameter, of the vaginal mucosa were excised from women who, with few exceptions, were patients in the gynecologic clinic. The vagina is a relatively insensitive organ and the pain connected with the biopsy-taking so slight and brief that many patients never complained of it. Anesthesia was never used. After the introduction of a bivalve

implant itself secondarily elsewhere continuing its growth in the new site. But such a view is hardly tenable, for it is evident that the embryo depends upon the maintenance of a free flow of maternal blood around its chorionic villi. When the trophoblast is confined in decidua, the embryo is nourished, but when the villi break their bounds, they become imbedded in blood clot and the embryo is in a short while asphyxiated. How can secondary abdominal or intraligamentous pregnancy then occur? It is manifestly impossible for an embryo once surrounded by coagulated blood to extricate itself when deposited in a fresh place and recommence its development. Whether tubal rupture or tubal abortion occur the fate of the embryo is sealed from the moment the perifetal coagulation starts. Hence the existence of an ovarian pregnancy, an abdominal pregnancy, or an intraligamentous pregnancy cannot follow on its extrusion from the tube but exists because it begins its development primarily in these sites.

SUMMARY

Various observers including ourselves, have demonstrated healthy endometrial tissue in tubal lumina. Sampson and Jacobsen, and others have proved beyond doubt that such endometrial tissue can and does implant itself and grow elsewhere displaying a preference for serous surfaces. Cases have been reported in the literature of endometrial tissue in the tubes. We have one such case.

Many observers have found decidual tissue in tubes whether or not they were the site of pregnancy. We have found it present at the site of the pregnancy in 62 per cent of casual specimens, in 87½ per cent of cases where we made a careful search and believe that it is present at the outset in 100 per cent of cases.

In one case we succeeded in finding endometrial glands in this decidual tissue, proving that the decidual reaction was caused by the response of endometrial elements and not the tubal structure itself. The fact that the fibrin layer of Nitabusch can be demonstrated in these ectopic decidual tissues shows that the ectopic endometrium carries out its functions as completely as when it was on the uterine wall.

The ectopic endometrial tissue was found in 1 out of 204 cases, an incidence of ½ per cent. The ratio of ectopic to intrauterine pregnancy is about 1 to 202 (Schumann's¹⁸ series) in Farrar's¹⁹ series 4 to 309, a significant correspondence of statistics and the explanation of the frequency of ectopic gestation.

CONCLUSIONS

1. All ectopic pregnancies, tubal or otherwise, occur because of nidation of the fertilized ovum in a locus of ectopic endometrial tissue to which the ovum is chemotactically attracted.

fication, in which the cells are very flat and stain deeply. (3) A basal zone in which the structure is much the same as in the stratum germinativum or malpighian layer of the epidermis. The basal zone is comparatively thick and shows a gradation in the character of its cells as one proceeds from the basement membrane toward the periphery. Roughly,

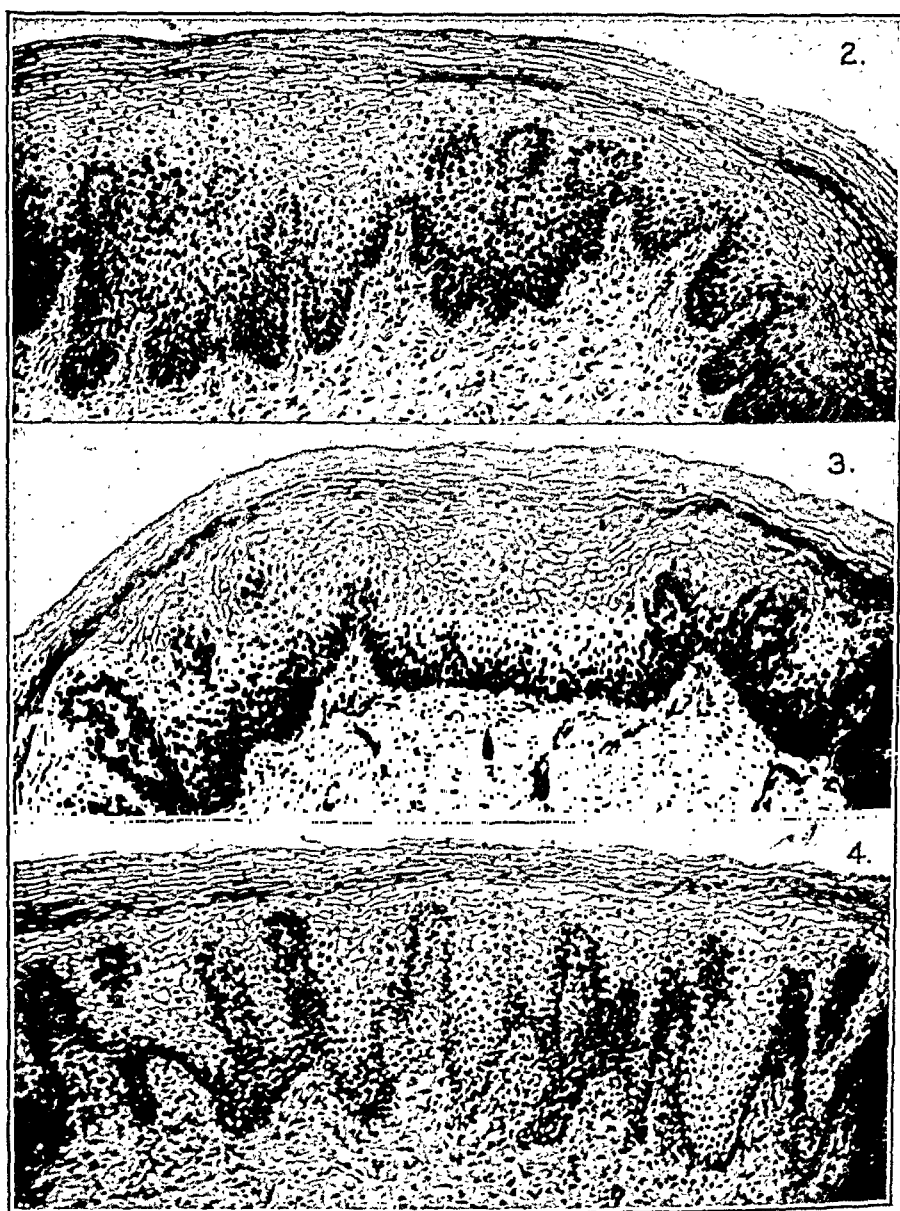


Plate I. Photomicrographs of sections of the vaginal mucosa in women with normal menstrual cycles, in the absence of pregnancy. $\times 100$. (After Smith and Brunner, 1934, *Am. J. Anat.*)

Fig. 2.—This section shows less than the usual amount of vacuolation in cells of the basal layer of the epithelium.

Fig. 3.—The amount of vacuolation here shown approximates the average.

Fig. 4.—The amount of vacuolation is a little above the average.

this zone may be subdivided into three layers: (a) A deep zone appearing, in sections, as a few rows of small cells in which the nuclei stain deeply. Cells of the row immediately adjoining the basement membrane

speculum a prominent mucosal fold was selected and punched with a Myle's cutting-edge fenestrated forceps. Upon withdrawal of the speculum, the folds of mucosa closed over and the minute wound collapsed leaving no bleeding surface. The slight wounds thus protected healed readily. The pieces were fixed in 10 per cent formalin, passed directly to 80 per cent alcohol and subsequently imbedded in paraffin. Serial sections were cut with a thickness of 10μ and stained with Delafield's hematoxylin followed by eosin.

In cases where the surface of the epithelium was folded, care was taken to orient the object so that sections would be cut transverse to the principal fold. Notwithstanding this care in orientation, some sections or portions of sections were found to be oblique. Such sections are misleading in that they tend to give an exaggerated idea of the size of cells that are more or less flattened. In the diagnosis of pregnancy, it is important to avoid oblique sections. Even a small amount of obliquity can be detected if the section cuts through some slender papillae.

The material for this investigation consists primarily of 155 biopsies from 79 cases of pregnancy and suspected pregnancy. Most of these biopsies are normal, but some are pathologic. The ages of the patients range from sixteen to forty-two

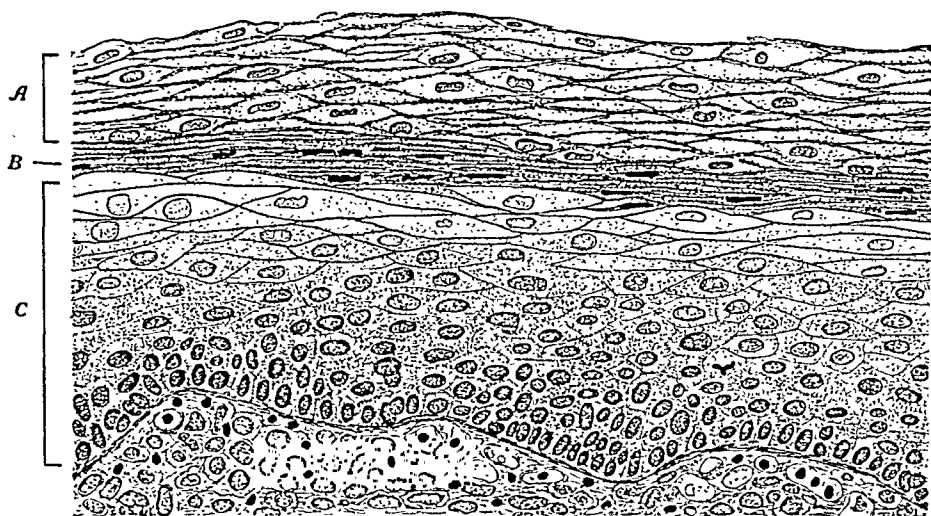


Fig. 1.—Drawing of a transverse section through the vaginal mucosa of a twenty-three-year-old nullipara, showing a portion of the epithelium overlying the summit of a papilla. $\times 540$. A, Superficial zone; B, middle zone or intraepithelial zone of cornification; C, basal zone. (After Smith and Brunner, 1934, *Am. J. Anat.*)

years. We have for comparison 118 normal biopsies from 49 women representing every phase of the menstrual cycle, also 41 pathologic biopsies from 19 women in various phases of the menstrual cycle. This material has been fully described in our previous paper, but will receive some attention here.

All the photomicrographs illustrating this article were made by Mr. Martin Haggett, using the same optical equipment throughout. The photographs were taken with a magnification of $\times 130$, and in the process of reproduction were reduced to $\times 100$.

TYPICAL STRUCTURE OF THE VAGINAL MUCOSA

The epithelium of the human vagina (Fig. 1) may be divided into three sharply defined zones or strata, as follows: (1) A superficial zone composed of moderately flattened cells that stain faintly with hematoxylin and eosin. (2) A middle zone, the intraepithelial zone of corni-

Even in normal mucosae, a considerable number of extravascular white blood corpuscles, usually lymphocytes, may be found in the layer of delicate connective tissue (lamina propria) underlying the basement membrane of the epithelium. These are shown as large black dots in Fig. 1. A slight amount of infiltration of leucocytes into the basal layer of the epithelium is a normal occurrence. In Fig. 1 only a single leucocyte, with distorted nucleus, is shown imbedded in the epithelium; but in an epithelial area of the size represented in the drawing, there would ordinarily be several leucocytes. The lamina propria contains numerous small blood vessels and small lymphatic vessels.

The structure thus described is fundamental, and in normal cases there are no essential differences when different regions of the same vaginal mucosa are compared. Nevertheless, the picture varies considerably depending on the presence or absence of papillae. Where papillae are absent throughout areas of considerable extent, the stratification is fairly uniform; where they are numerous, as shown in most of the figures illustrating this paper, the basal zone is much thicker between the papillae. This increased thickness is due to an increase in the number of clear cells and polyhedral cells. Differences correlated with the phases of the menstrual cycle are slight and need not concern us here. When normal mucosae from different individuals are compared, the chief differences are those relating to the degree of development of the intraepithelial zone of cornification and to the number and size of the clear cells. We are here concerned mainly with the clear cells, since the cells of the clear zone are especially large and numerous during pregnancy.

We have previously studied the clear cells in 118 normal biopsies from 49 women in various phases of the menstrual cycle (Smith and Brunner, 1934). After a preliminary examination of these biopsies to determine the largest amount of vacuolation present in any of them, all were graded with respect to the amount of vacuolation, on a scale of five. (In the present paper, Grade 1 is illustrated by Fig. 2; Grade 2 by Fig. 3; and Grade 3 by Fig. 4). The average for the 118 biopsies is 2.41. In the entire series, Grade 5 was assigned to only seven biopsies from five patients. Since Grade 5 is rare, it may be due to the operation of some unusual factor. It is possible that the five patients were in a very early stage of pregnancy. All the dates for the seven biopsies fall within twenty-six days of the beginning of the preceding menstrual flow, but we do not know whether the supposed cycles were terminated by menstruation.

PATHOLOGIC MODIFICATIONS

In normal material taken at any stage of the menstrual cycle, there is considerable variation in the number and size of the clear cells in different individuals (Figs. 2 to 4), but the clear zone is always present. In

are usually columnar; the others are cuboidal or polyhedral. (b) A zone of rather large polyhedral or slightly flattened cells that stain moderately. (c) A zone of clear, slightly flattened, highly vacuolated cells that stain faintly. Peripherally, this zone is sharply bounded by the zone of intraepithelial cornification.

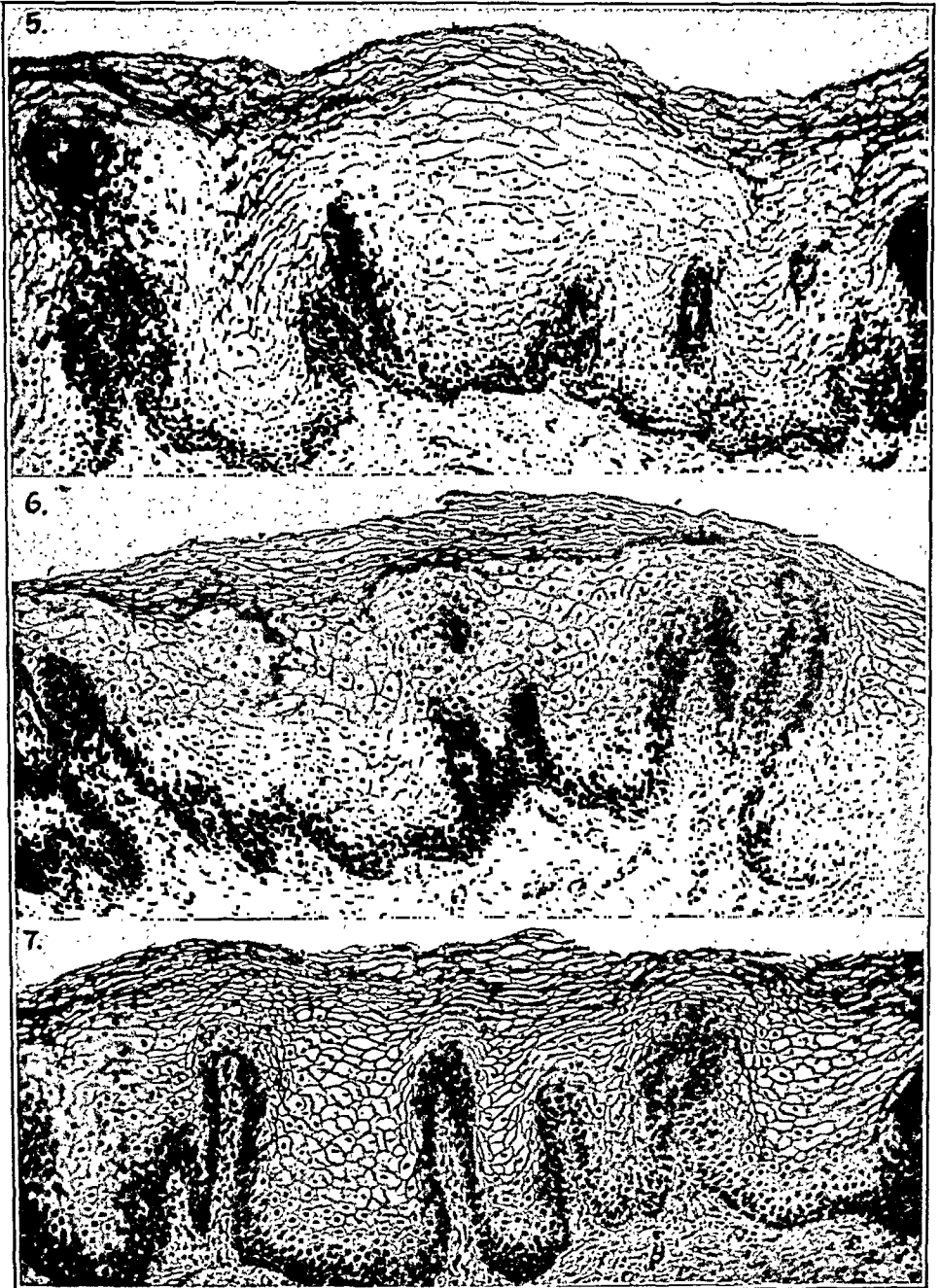


Plate II. Photomicrographs of sections of the human vaginal mucosa in early stages of pregnancy. $\times 100$.

Fig. 5.—Approximately three weeks pregnant (menstrual flow six days overdue). The amount of vacuolation is slightly above the average for the first month.

Fig. 6.—Approximately six weeks pregnant (menstruation thirty-two days overdue). The amount of vacuolation is above the average for the second month.

Fig. 7.—Approximately eight weeks pregnant (menstruation forty-five days overdue). The amount of vacuolation is only slightly above the average for the second and third months.

THE VAGINAL MUCOSA IN PREGNANCY

In our previous investigation (Smith and Brunner, 1934) we were impressed by the increase in vacuolation of the cells of the distal portion of the basal zone during pregnancy. Not only do the clear cells increase in size, but the clear zone extends almost to the deep layer of darkly staining cells (as in Figs. 5 to 7 of the present paper). This increase did not occur in material that was obviously pathologic. Our normal material taken during pregnancy consisted of 48 biopsies from 20 pregnancies ranging in duration from approximately three weeks to the eighth lunar month inclusive. In order to facilitate comparisons, we attempted to grade these biopsies with respect to the amount of vacuolation in the basal layer, using the scale employed for the study of vacuolation during the menstrual cycle. It was necessary to increase the range of this scale from five to six, in order to make it applicable to all biopsies taken during pregnancy. (In the present paper, Grade 6 is illustrated by Figs. 5 to 7, though the amount of vacuolation shown in Fig. 7 is barely sufficient to justify a grade higher than five.) The general average for the 48 biopsies from 20 pregnancies was 4.96, which should be compared with the general average of 2.41 for 118 normal biopsies from 49 women in various phases of the menstrual cycle.

In what follows, all biopsies obtained during our earlier study of pregnancy are incorporated with our later material. At present, our material consists of 155 biopsies from 79 cases of pregnancy and suspected pregnancy. Of these, 33 biopsies from 26 patients are obviously pathologic and of no value for diagnosis. The fact that the amount of vacuolation in these specimens is small (in some instances clear cells are entirely absent) should not be interpreted as negative evidence; for, as previously explained, even a moderate inflammation usually inhibits vacuolation. Nevertheless, from nine of these patients partially normal biopsies also were obtained; these are included in the normal group to be described presently. Thus, out of 79 patients, 17, or 21.5 per cent, furnished exclusively pathologic biopsies. Of this group 12 patients (one ectopic pregnancy) were definitely pregnant, 2 were not pregnant, and 3 remained doubtful since the clinical evidence was inconclusive and the patients did not return for reexamination. The ages of these patients ranged from seventeen to forty-two years.

There remain for consideration 122 normal or nearly normal biopsies from 62 cases of pregnancy and suspected pregnancy. The ages of these patients range from sixteen to forty-one years. In estimating the duration of pregnancy, the twelfth day of the menstrual cycle is taken as the most probable date of conception. On this basis, every lunar month of pregnancy excepting the tenth is represented in the biopsies. In the earliest case of suspected pregnancy, menstruation was one day overdue. There are 18 cases where menstruation was not more than twelve

cases of chronic vaginitis the formation of the clear zone is partially or wholly suppressed, save that one may occasionally find normal areas in which the clear zone is well developed. Since even a moderate degree of inflammation is sufficient to prevent the increase in size and number of the clear cells characteristic of pregnancy, it is important to be able to recognize the other structural modifications associated with vaginitis.

In mild vaginitis, of whatever origin, there is moderate hyperemia with little or no extravasation of blood, more than the usual number of leucocytes in the tunica propria, marked infiltration of leucocytes into the basal layer of the epithelium, and a blurring of the boundaries of the polyhedral cells. The layer of clear cells, the zone of cornification and the superficial zone appear almost normal. In moderate or severe vaginitis of a chronic nature, the histologic modifications extend to the zone of cornification and even to the superficial zone. Nevertheless, one may find localities where the structure is almost normal, while in other portions of the same biopsy, or in other biopsies from the same mucosa, the pathologic modifications are quite obvious. We shall now describe the usual effects of chronic inflammation on the structure of the vaginal mucosa, layer by layer.

In many instances the superficial zone tends to resemble the zone of cornification. In severe cases the superficial zone is dense and its cells are greatly flattened; it undergoes desquamation in scalelike masses of cells, and may be entirely lacking (in sections). The zone of cornification is usually thicker and is always denser than in its normal state; it may be almost homogeneous. This is often the most striking indication of chronic vaginitis. In all cases the layer of clear cells suffers reduction in some degree. In severe cases there is not only entire absence of clear cells, but there is a reduction in the number and size of the pale, slightly vacuolated cells that normally underlie the clear cells. The layer of polyhedral cells is unusually dense and may extend quite to the zone of cornification. Somewhat rarely, the layer of clear cells is replaced by a stratum granulosum.

Characteristically, there is a decided increase in the number of leucocytes in the lamina propria, especially in the papillae, and a corresponding increase in the amount of infiltration of leucocytes into the basal layer of the epithelium. Nevertheless one may find, in a portion of the mucosa where the number of leucocytes is not excessive, all the other modifications characteristic of chronic vaginitis.

Usually, the blood vessels are distended and there is some extravasation of blood into the connective tissue. Caution is needed in interpreting this as evidence of hyperemia, for it may be an artifact. In many cases the extravasated blood within a papilla crowds the other tissues aside, forming a small hematocele with a sharply defined spherical boundary. This enlarges at the expense of the epithelium, and in extreme cases may extend almost to the periphery.

strual cycle, from 49 patients. Thus it appears that the amount of vacuolation is approximately twice as great during pregnancy.

It is known that the epithelium of the vaginal mucosa is normally rich in glycogen. In thirty women with normal menstrual cycles and normal vaginal mucosae, Niderehe (1923) found the glycogen content highest during the premenstrual stage. On the other hand, Gisbertz (1929 and 1930) found great variation in the glycogen content, but concluded that the variations were not cyclical in character. Gisbertz believes that the intracellular vacuoles visible in ordinary preparations of the vaginal epithelium are filled, during life, with glycogen in liquid form. Our own studies (Smith and Brunner, 1934) indicate that variations in the amount of glycogen are not related to the menstrual cycle.

Niderehe (1923) stated that there is an increase in the amount of glycogen during the early stages of pregnancy, and a gradual decrease during the later months. It would be interesting to know if the same rule holds for vacuolation. Using our 110 normal or nearly normal biopsies from 54 patients with a histologic diagnosis of pregnancy, we computed the average amount of vacuolation for each lunar month represented. The results are shown in Table I. The slight drop in vacuolation indi-

TABLE I. AVERAGE AMOUNT OF VACUOLATION IN CELLS OF THE BASAL ZONE OF THE VAGINAL EPITHELIUM FOR EACH OF THE FIRST NINE LUNAR MONTHS OF PREGNANCY. BASED ON 110 BIOPSIES FROM 54 WOMEN.
THE GENERAL AVERAGE IS 4.98

LUNAR MONTH	1	2	3	4	5	6	7	8	9
No. of patients	14	20	9	6	1	1	1	1	1
No. of biopsies	25	39	19	13	7	3	1	1	2
Vacuolation	5.48	4.82	4.84	5.00	5.00	5.33	5	5	5

cated for the second month may be significant, and there is no change during the third month; but in the later months the number of cases is too small to be of much use in this connection. Lewis (1935) described and illustrated (photographically) a high degree of vacuolation of the vaginal epithelium at the very end of pregnancy, the time of delivery.

DISCUSSION

The principal defect in our method for the diagnosis of pregnancy is that it is not applicable to cases exhibiting marked pathologic modifications of the vaginal mucosa. In chronic vaginitis, the formation of intracellular vacuoles, upon which the histologic method of diagnosis depends, is inhibited. For this reason, in about one-fifth of our cases a diagnosis by this method was impossible. It is probable that in private practice the proportion of pathologic cases would be lower.

It is pertinent to consider some other conditions that might make a histologic diagnosis difficult or impossible. In our previous contribution

days overdue; according to the mode of reckoning employed, these fall within the first month. There are 24 cases for the second month. Thus, 67 per cent or about two-thirds of the total number of cases from which normal biopsies were obtained fall within the first two months of pregnancy or suspected pregnancy.

In 7 cases of suspected pregnancy, with menstruation from one to seventeen days overdue, the histologic diagnosis was negative. These cases were represented by 10 biopsies. At later clinical examinations six of these patients were found not pregnant; the other patient did not return. In a single patient (thirty-eight years of age, menstruation forty days overdue) the histologic diagnosis based on two biopsies was doubtful. Seven weeks later, this patient was reported not pregnant.

In 54 cases, represented by 110 biopsies, the histologic diagnosis was positive. In 47 of these cases a clinical diagnosis of pregnancy was made at the time of biopsy; in the remaining 7 cases, pregnancy was merely suspected. Since approximately two-thirds of the 54 cases fall within the first two months of pregnancy, it is important to note any evidence obtained from later clinical examinations. In 14 cases, menstruation was from six to twelve days overdue; these cases are assigned to the first month of pregnancy. Ten of these patients were examined at a later date and pronounced pregnant; the other 4 did not return. In 20 cases menstruation was from thirteen to forty days overdue; these cases are assigned to the second month of pregnancy. Of this group, 8 patients returned for examination and were pronounced pregnant; the others did not return. Of the remaining 20 patients, in later stages of pregnancy, only five returned for examination and in these cases the diagnosis of pregnancy was confirmed. Thus, all the clinical evidence available supports the histologic diagnosis of pregnancy.

It is of interest to note that a histologic diagnosis is possible in a very early stage of pregnancy. In 4 cases a positive diagnosis was made when menstruation was only six days overdue; in 2 of these cases the diagnosis was confirmed by a later clinical examination. In 2 cases a positive diagnosis was made when menstruation was eight days overdue; both diagnoses were confirmed by later clinical examinations. In one of the latter cases there was a history of a single intercourse three weeks before the biopsy was taken.

Some comparisons with biopsies taken during the menstrual cycle are in order. In all the biopsies taken during pregnancy or suspected pregnancy, the amount of vacuolation in the basal layer of the epithelium was graded on a scale of six. In the 110 biopsies from 54 cases in which the histologic diagnosis was positive, the average amount of vacuolation is 4.98. The general average for the menstrual cycle is 2.41; this is based on 118 normal biopsies, well distributed throughout the men-

we would emphasize the advantage of preparing an entire series of sections of each biopsy; for in mucosae that are mainly pathologic, normal areas may sometimes be found.

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CIRCULATION TIME STUDIES IN PREGNANT WOMEN

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OUR purpose in reporting circulation time studies in pregnancy is to supply additional data relative to the changes which occur during normal gestation.

It has been generally accepted that during normal pregnancy the work of the heart is increased. This is evidenced by an increase in minute volume output of the heart, increase in circulating blood volume, increase in basal metabolic rate, increase in ventilation and diminution in vital capacity.

Lindhard,¹ Stander and Cadden,² Haupt,³ Schmidt,⁴ Schroeder,⁵ Anthony and Hansen⁶ have shown that the minute volume output of the heart increases, from a minimum of 15 per cent to a maximum of 74 per cent from the fourth month of pregnancy onward. The increase in cardiac output is due to increased venous return and greater diastolic filling of the auricles. In accordance with Starling's law, the increased venous return causes a greater stretching of the heart muscle during diastole, and a consequently greater stroke volume output.

In addition to the increased venous return, Dieckmann and Wegner,⁷ Schoenholz,⁸ and others have shown an increase in the volume of circulating blood, with an increase in plasma, a relative or absolute diminution in the number of formed elements, and a relative anemia.

Plass and Yoakum⁹ have shown a progressive increase in the basal metabolic rate from the fourth month of gestation to term and a subsequent fall during the puerperium. Boothby and Plummer¹⁰ have shown that there is a greater amount of energy expended per unit of work in those with elevated basal metabolic rates than in those with normal rates.

Krukenberg¹¹ showed that following a measured amount of work, the blood pressure in pregnant women rose higher than in nonpregnant women, and was slower in returning to normal. The pulse rates of the pregnant women were more rapid than could be accounted for by the increase in work.

The ventilation rate has been shown by Eismayer and Pohl¹² to be increased, while the vital capacity is diminished. They also found a slight elevation of pulse and blood pressure in pregnancy.

(Smith and Brunner, 1934) we stated that in pathologic amenorrhea (represented by 19 otherwise normal biopsies from 5 patients), the amount of vacuolation is greater than during the menstrual cycle, but decidedly less than during pregnancy. The number of cases is too small to enable an unqualified conclusion to be drawn. We can see no reason why vacuolation should be increased during pathologic amenorrhea. Nevertheless, in view of the facts stated it seems possible that in occasional cases of pathologic amenorrhea the amount of vacuolation might be large enough to be confusing.

We have stated (Smith and Brunner, 1934) that during and after the menopause the distal portion of the basal zone (in 7 fairly normal biopsies from 7 patients) is rather highly vacuolated, but we were careful to add: "Niderehe (1923) states that after the menopause there is a decrease in the amount of glycogen associated with a lessened height of the vaginal epithelium. We do not know whether the intracellular vacuoles found in our sections represent spaces filled, during life, with glycogen, but the cytological appearance is not quite the same as it is during the child-bearing period." This important qualification appears to have been overlooked by Lewis (1935) in his references to our article. Perhaps we should be more explicit. We are by no means assured that the vacuolation found after the menopause is entirely homologous with that present during the menstrual cycle and during pregnancy. It seems, in part, to be a consequence of involution—a result of the increasing poverty of cytoplasm accompanied by an actual decrease in secretory function. Better fixation and the use of special stains are needed to settle this question.

When, in 1929, we began our studies on the structure of the vaginal mucosa, it was in search of a method for the diagnosis of pregnancy. Meanwhile, other tests for pregnancy have come into general use. This should not entirely preclude the use of the method here described. For various reasons, it is well to have several methods available. As compared with the Aschheim-Zondek and the Friedman tests, the histologic method has the advantage of rapidity. The biopsies are small and the usual paraffin technic can be speeded up so that the sections are ready for study in a very few hours. We hope that some one will test this method in a sufficient number of cases of ectopic pregnancy, where the time factor is important.

In this paper considerable attention has been given to conditions that may defeat an attempt at a histologic diagnosis. This should not obscure the fact that, in normal cases, the method is almost uniformly successful. Often, a single glance at a preparation under the low power of the microscope enables one to make an unqualified decision. However,

the examiner detects the odor of ether. This measures the arm-lung time or the passage of blood through the right heart as far as the arterial capillaries of the lung.

Normal figures for the tests in nonpregnant women are as follows: from eight to sixteen seconds for arm-tongue time, and four to eight seconds for arm-lung time.

For subjects we selected thirteen normal pregnant women from the Morrisania City Hospital antepartum clinic. At monthly intervals, beginning as early as the third to the fifth month of gestation, we did arm-lung and arm-tongue determinations. Blood pressure and pulse rates were taken, urinalyses and physical examinations were done at the same time. Both multiparas and primiparas were included. We feel that there is no danger in this procedure. Fishberg, speaking before the Section of Medicine at the New York Academy of Medicine, stated that several hundred such determinations have been made with no untoward effects. In our series of 52 arm-tongue and 58 arm-lung determinations, only on three occasions did thrombosis of the antecubital vein occur. There were no other complications.

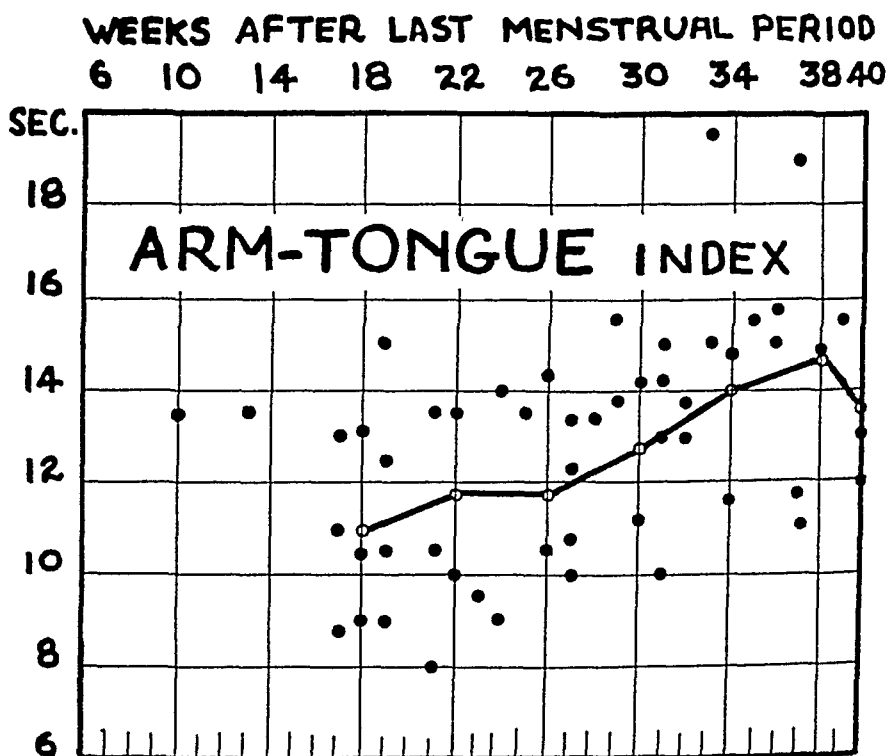


Chart 1.

RESULTS

There were 52 determinations of arm-tongue time done on 13 patients (Table 1). The minimum time was eight seconds in the twenty-first week of gestation and the maximum was 19.4 seconds in the thirty-third week. All patients except Cases 2 and 8 showed an increase in the circulation time as gestation progressed. There was only 1 determination in Case 2. Chart 1 contains all the arm-tongue determinations represented by black dots, with the average for each month represented by a circle. The average arm-tongue time shows a progressive increase, from 10.9 seconds at the eighteenth week of gestation until it reaches a maximum of 14.7 seconds at the thirty-eighth week of gestation. There is a drop to 13.5 seconds at the fortieth week of gestation.

There were 58 determinations of arm-lung time on the same 13 patients (Table I). The minimum time was 2.8 seconds obtained in the seventeenth and twenty-sixth

Dyspnea on exertion and easy fatigability, the early symptoms of cardiac decompensation, are of frequent occurrence. Signs of cardiac disturbance, such as tachycardia, premature contractions, and even transient auricular fibrillation may occur in normal pregnancy.

These findings would all seem to corroborate the concept that the heart works harder and less efficiently in pregnancy.

We felt that if the heart did perform less efficiently, this might be reflected in the progressive prolongation of the circulation time during the course of pregnancy. Blumgart¹³ showed that there is a definite correlation between speed of circulation and functional capacity of the heart.

The determination of the speed of circulation by the introduction of a foreign substance into the blood stream at one point, detecting its presence at another, and measuring the elapsed interval is a procedure that has been known for many years.

Blumgart¹⁴ has summarized completely the various methods employed, and with the use of radioactive substance revealed the great value of this method in studying the circulation in normal and abnormal states.

Harrison's¹⁵ careful studies have shown that in a failing myocardium, symptoms and signs are due to "backward failure" which results in an accumulation of blood in the lungs from left heart weakness, or congestion of the liver and peripheral edema in right heart failure. Such slowing of the circulation would tend to slow up any foreign substance present in the blood stream.

Despite any symptoms of cardiac weakness, such as dyspnea and easy fatigability, the finding of a normal circulation time effectively rules out the presence of cardiac failure. It is possible by circulation time studies to determine not only the efficiency of the whole heart, but also of the right and left components.

We have selected the method devised by Fishberg, Hitzig and King¹⁶ for our determinations. It is true that the method is not entirely objective, but Hitzig¹⁷ has shown that though the time may vary from one individual to another there is very little change in the same individual. He found that repeated tests in 22 cases showed a variation of 0.5 to 2.0 seconds. Consequently, we may accept this test to be quite accurate.

PROCEDURE

With the patient at rest for at least one-half hour, a solution of 3 gm. of saccharine (gluside) is dissolved in 3 c.c. of sterile distilled water, and then injected rapidly into the ante-cubital vein through an 18-gauge needle. The patient has been instructed to announce when a sweet taste is first detected at the base of the tongue. Timing begins from the first drop injected. This is the arm-tongue time and measures the passage of blood through the right and left sides of the heart.

With the needle in situ, the syringe is removed and replaced by one containing 3 c.c. of a freshly prepared 10 per cent solution of ether in sterile distilled water. The patient is instructed to exhale forcefully, and the solution is rapidly injected. The time is measured from the beginning of the injection until the moment when

TABLE I

CASE	PARITY	PERIOD OF GESTATION IN WEEKS	CIRCULATION TIME IN SECONDS	
			ARM-TONGUE	ARM-LUNG
1	iv	10	13.6	5.6
		19	15.0	6.8
		24	14.0	4.2
		29	13.8	6.0
		33	19.4	6.8
		37	19.0	6.8
2	ii	19	12.4	6.0
		25		6.8
3	0	19	9.0	5.4
		27	10.0	5.0
		32		5.6
		37		5.0
		40	12.0	7.0
4	iv	13	13.0	5.0
		18	10.5	4.0
		22	10.0	4.0
		26		2.8
		30	14.2	3.6
		39	15.6	4.2
5	ii	21	8.0	4.0
		26	10.5	5.0
		30	11.4	4.8
		34	11.8	5.5
		38		6.5
6	ii	17	13.0	3.8
		21	10.6	3.0
		27	12.2	2.8
		32	13.8	3.5
		37	11.2	5.2
		28	13.2	5.6
7	viii	32	13.0	5.0
		36	15.0	4.0
		18	13.2	6.8
8	iii	22	13.4	6.8
		26	14.2	
		31	10.0	3.6
		35		5.4
		18	9.0	3.0
9	0	23	9.4	3.2
		27	13.6	3.6
		31	15.2	3.2
		35	15.6	6.8
		17	10.8	3.4
10	0	22		4.0
		27		4.8
		31	14.2	5.2
		17	8.8	2.8
11	0	24	9.0	3.0
		33	15.0	4.8
		37	11.8	4.8
		19	10.6	2.4
12	0	25	13.4	5.0
		29	15.8	5.0
		34	14.6	5.4
		38	14.6	4.8
		21	13.4	
13	0	27	10.6	3.4
		31	13.0	5.0
		36	15.8	4.2
		40	12.0	5.0

weeks of gestation. The maximum time was 6.8 seconds obtained in the eighteenth, nineteenth, twenty-second, twenty-fifth, thirty-third, thirty-fifth, and thirty-seventh weeks of gestation. All patients except Cases 4, 7, and 8 showed an increase in the arm-lung time as gestation progressed. Chart 2 contains all the arm-lung determinations represented by black dots, with the average time for each month represented by circles. With the exception of a slight drop of 0.5 second at the twenty-second week of gestation, there is a progressive increase in the average time. Beginning with 3.9 seconds at the eighteenth week of gestation the arm-lung time increases to 5.4 seconds at the fortieth week.

It is apparent, then, that there is a slight but definite slowing of the velocity of blood flow through the lungs. Despite the increase in arm-tongue and arm-lung times, however, these times are still within normal limits. This is in contrast to the findings of Klee.¹⁸ He used Koch's¹⁹ fluorescein method, where the normal average circulation time is 20.8 seconds. He found in normal primiparas and multiparas

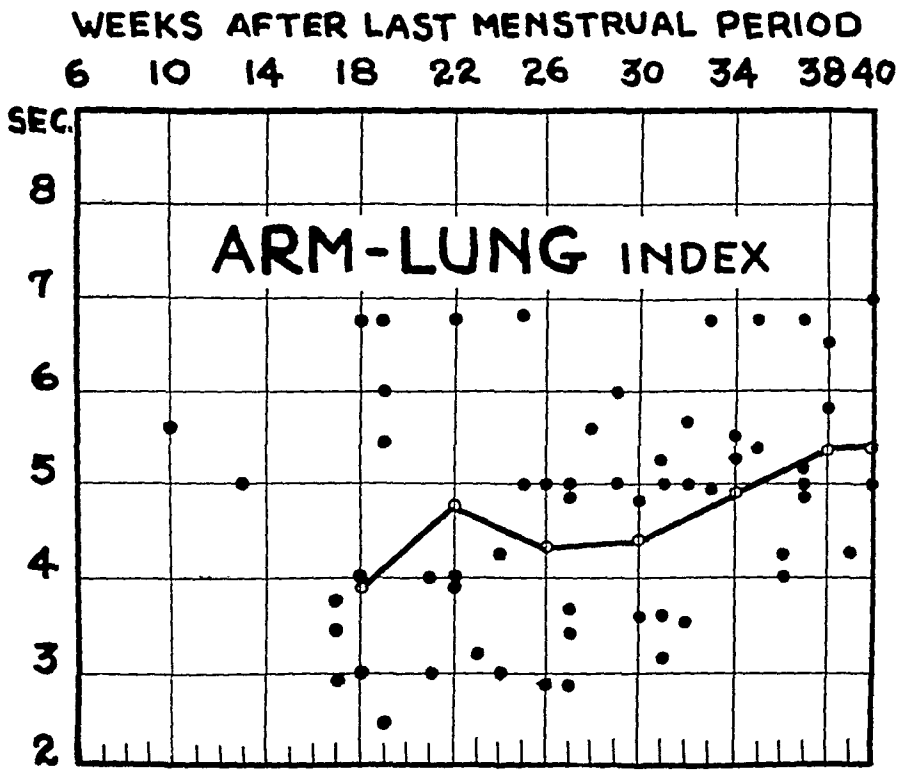


Chart 2.

increases over the normal ranging from 2.6 seconds to 6.4 seconds, in the last three months of gestation. However, we found, as he did, a slight decrease in time in the last two weeks of pregnancy. He ascribed this decrease to the lowering of the diaphragm with the descent of the fetus into the pelvis, allowing for greater thoracic space and better circulation. Spitzer²⁰ used the decholin method of Winternitz, Deutsch, and Brüll,²¹ which is similar to the saccharin method we employed. He found increases in circulation time during the latter part of pregnancy, but he did not follow his cases from month to month.

DISCUSSION

Blumgart²² showed that the greatest part of the time required for the blood to pass from the antecubital vein through the right and left sides of the heart is consumed in the lung capillaries, the other com-

increased blood volume (Thompson²⁹) and increased capillary bed from vasodilatation (Blumgart³⁰). Anselmino and Hoffman³¹ have attributed the changes in pregnancy to an increased secretion of the thyrotropic hormone of the anterior pituitary gland. There is very commonly in pregnancy a definite, palpable and visible increase in the size of the thyroid gland.

In spite of these similarities, there are several differences which should be pointed out. Most marked is the shortening of the circulation time in hyperthyroidism and the progressive increase of time in our series. The flushed moist warm skin in hyperthyroidism indicates the marked vasodilatation present. Despite the increase in cross-section of the vascular bed from vasodilatation, however, the circulation time is shortened and the rate of flow accelerated, showing the additional strain thrown on the heart by the abnormal stimulation.

In addition, we may point out that the progressive elevation of the basal metabolic rate in normal gestation, as noted by Plass and Yoakum,³² is almost within normal limits, in contrast to the abnormally high basal metabolic rate in hyperthyroidism. Also, enlargement of the thyroid in pregnancy is due to increase in the colloid and not due to hyperplasia. Hyperthyroidism, therefore, cannot be used to explain the presence of dyspnea and easy fatigability in pregnancy.

Harrison³³ was able to produce dyspnea and diminished vital capacity by injecting blood into the pulmonary artery of dogs. He attributed the dyspnea to a vagal reflex excited by pulmonary congestion. This factor may also be responsible for the dyspnea in pregnancy. Krukenberg's³⁴ studies of blood lactic acid in pregnant women revealed a delay in the resynthesis of lactic acid to glycogen. Physiologists attribute fatigue to the accumulation of metabolites in the tissues, chiefly lactic acid, which are not adequately oxidized. According to Meyerhof's theory of oxidation, a portion of the lactic acid produced is completely oxidized, the energy produced being required to resynthesize the remaining lactic acid to glycogen. Insufficient oxygen hampers this resynthesis. Apparently, therefore, there is a failure in the respiratory function rather than in the circulatory. In addition, the relative anemia is responsible for less oxygen absorption in the lungs and therefore diminished oxygen transportation to the tissues.

CONCLUSION

1. By means of circulation time studies, it is possible to demonstrate a slight but progressive retardation of flow of blood in the course of pregnancy.

2. The symptoms and signs which simulate cardiac weakness in the course of pregnancy may be due to increased pulmonary congestion and may be of respiratory rather than cardiac origin.

We are indebted to Dr. Harry Aranow, Director of Obstetrics and Dr. Sol Biloon of the Department of Medicine, Morrisania City Hospital, for their encouragement and advice. We also wish to thank Miss Hildegard Boucher for her assistance.

ponents being negligible factors. In other words, circulation time really measures the time required for the passage of blood through the lungs, and increase or decrease in time reflects a corresponding alteration in the speed of pulmonary circulation. Blumgart and Weiss²³ have shown that this time is independent of venous pressure, of vital capacity, of blood pressure, and only slightly affected by changes in the pulse rate.

Circulation time is related to cardiac output according to the formula which Stewart²⁴ derived in measuring blood flow through the lungs. This formula is $V = \frac{Q}{T} \times 60$, where V is volume output per minute in liters, Q is the quantity of blood in the lungs, and T is the mean pulmonary circulation time in seconds. It has been mentioned that the cardiac output increases progressively from the fourth month of gestation onward, which coincides with the increase in circulation time which we have found.

It is apparent from the equation that if V is to increase, Q must also increase or T diminish. That Q is increased can be deduced from the following facts. In the first place, with increased cardiac output, and slowing of the circulation as evidenced by progressive increase of arm-tongue time, it is obvious that there must be a greater amount of blood in the pulmonary capillaries. Second, there is a diminished vital capacity which is not sufficiently explicable on the basis of an elevation of the diaphragm. Alward²⁵ made vital capacity determinations before and after removing a huge ovarian cyst containing 15,000 c.c. of fluid and found no difference in vital capacity. Lemon and Moersch²⁶ have had similar results with ovarian cysts. That it is due to increased amount of blood in the lung capillaries, diminishing the alveolar spaces, is substantiated by the experimental studies of W. G. Harrison, Jr., Calhoun, Marsh, and T. R. Harrison.²⁷ They produced pulmonary congestion artificially and found vital capacity diminished correspondingly. On the other hand, rather than finding T diminished, we found it to increase progressively.

The great increase of circulation, through the viscera, particularly the uterus, causes a marked increase in the capillary bed. In a rigid tube system, the rate of flow is inversely proportional to the cross-section of the tube. This is not exactly applicable to the human system, which can undergo wide variations; but in view of the definite increase in capillary bed, the rate may be considered as diminishing according to the equation $V = \frac{a}{\pi r^2}$, where V is the rate of flow, a the volume of flow and r the radius of the tube corresponding to the cross-section of the capillary bed.

These physiologic changes of increased volume output, increased blood flow through the lungs and diminished vital capacity in pregnancy are present in hyperthyroid states. In hyperthyroidism there is a diminished vital capacity (Rabinowitch²⁸), increased ventilation rate,

Duzen in his cystoscopic studies of cystoceles and his anatomic studies of the female trigone muscle, in collaboration with William W. Looney in the Department of Anatomy, Baylor School of Medicine, Dallas, Texas. These investigators give credit to Young and Wesson for their description of the male trigone and supplement this study with their work on the female trigone muscle.

This trigone muscle is a thin triangular sheet in the base of the bladder, bounded above by Mercier's bar, and below by the internal orifice of the urethra through which its fibers loop to fasten in the posterior wall of the urethra for a distance of approximately one-half the latter's length. The lateral margins of the trigone muscle are somewhat thickened and are called Bell's muscles. The trigone is covered with a smooth mucous membrane closely adherent to the underlying muscle coat, thus forming a smooth, firm platform, even when the remainder of the empty bladder is in folds.

In women with normal bladders, the ureteral orifices are about 3 cm. apart and 3 cm. above and behind the internal sphincter, the urethra being approximately one to one and one-half inches long. Bladder injury may make this distance vary with the location and extent of the injury, the tendency being to make the distance greater in injury below Mercier's bar, whereas damage above Mercier's bar shortens this distance. In some cases, the cystocele may involve tissues both above and below Mercier's bar.

In the female, Van Duzen and Looney find that the internal sphincter consists of "two portions, namely inner and outer," and "the most internal fibers form a complete sphincter around the internal orifice of the urethra," while "the outer portion of the inner bundle appears to loop partially around the urethral orifice. The outer portion of the sphincter lies external to and somewhat below the inner portion;" the fibers begin on the posterior wall and pass on each side of the urethral orifice to its anterior surface. The external portion extends down the urethra to the urogenital diaphragm. Thus we have a loop muscle arrangement extending from the internal sphincter bladder surface to the urogenital diaphragm, and it is through this aperture that the trigonal muscle passes to be attached in the urethra. Young showed that the internal sphincter is opened by the downpull of the trigonal muscle, passing in the form of a bow through the weaker arcuate muscles, comprising the internal sphincter, at the vesical orifice (see Fig. 7). When the trigonal muscle is torn near the point at which it passes through the internal sphincter, this latter circular muscle is released from the effects of the downward pull occasioned by voiding, and in consequence of this release, internal sphincter spasm occurs. Long duration of this spasm invites mucosal hyperplasia on the contacting surfaces of this released internal sphincter. A vicious circle is now established in that the hyperplastic urethral tabs irritate the

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1147 HOE AVENUE

15 EAST CLARKE PLACE

A NEW OPERATION FOR CYSTOCELE*

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THE repair of cystocele has frequently in the past given satisfactory results from a gynecologic viewpoint, only to leave considerable dysuria. Analyses of the types proving unsatisfactory were found to be those in which the urethra was severed from the trigonal muscle. This type of cystocele may be innocuous looking from the exterior, but its full extent is best appreciated on cystoscopic examination. It is our effort to recognize and repair this particular type, thus restoring the pelvic floor anatomically, and the bladder functionally, to a condition as nearly normal as possible.

The anatomy of the female bladder and urethra has received limited attention in textbooks, except in that of Kelly and Burnam, and efforts to review this phase of the subject have usually revealed relatively little of its physiology. Attention is directed to the importance of an intact supporting pubocervical fascia and the necessity of keeping the cervix uteri elevated to maintain normal position and relations.

The best information for the gynecologist on the anatomy and physiology of the female bladder was found in the work of Rex E. Van

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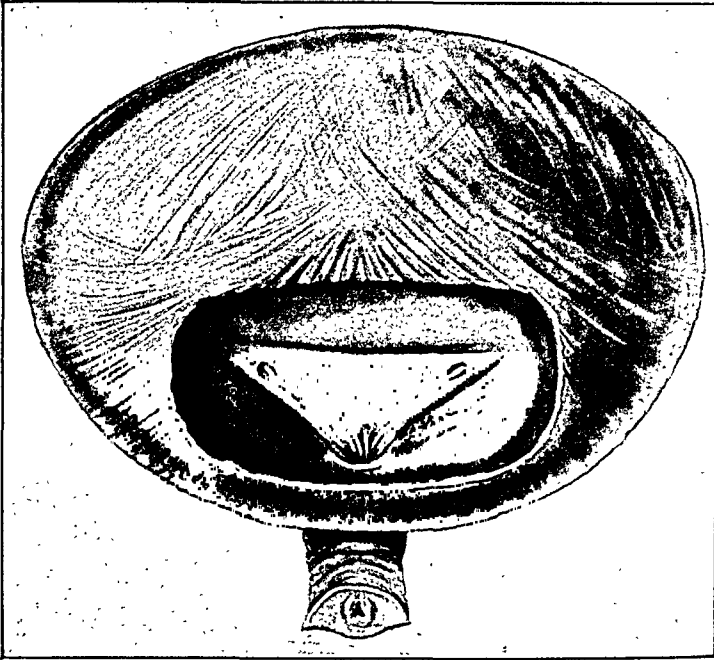


Fig. 2.—Anterior view of distended bladder exposing trigone and base of bladder. (From Kelly and Burnam.)



Fig. 3.—Diagrammatic representation of normal curve of urethra, trigone, and bladder floor. (Modified after Kelly and Burnam.)

sphincter to greater contraction. It is this sequence of events that particularly may account for bladder irritability, even in the absence of a cystitis. Such an injury to the trigone muscle causes a delay in starting the stream and necessitates straining, because the sphincter must now be opened by increased intravesical pressure rather than by the trigonal muscle.

The majority of cystoceles observed are damaged near the point of fascial attachment between the cervix and bladder, that is, above Mercier's bar, where any standard plastic repair that elevates the cervix and supports the bladder floor will effect a cure. However, there is a relatively small percentage of cases in which the trigone muscle is damaged or sheared off from the internal sphincter, the injury being below Mercier's bar, and permanent cures are relatively rare. It is for this particular type of cystocele that we now suggest this method of anatomic repair and restoration of physiologic func-

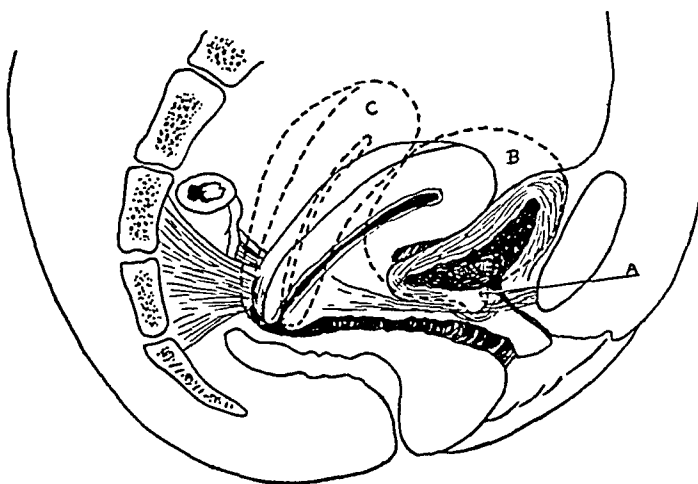


Fig. 1.—Uteropubic fascia and uterosacral ligaments. Schematic drawing of this particular type of cystocele (*A*) when bladder is distended (*B*) displacing corpus uteri (*C*). (From Fairar in Curtis' *Obstetrics and Gynecology*.)

tion, which consists in functionally reuniting the severed, or partially severed, portions of the trigone muscle above the internal sphincter with that small portion which is anterior to the internal sphincter and which serves as its attachment in the urethra. In the main, this is done by first drawing these two portions together near the internal sphincter with sutures parallel to the long axis of the urethra, and then supplementing this functional repair by splinting these two portions with tissue from beneath the anterior urethra to the posterior area of the trigone. This fascial splinting is carried to the uterine body as in the standard advancement operations described in textbooks by Crossen, Curtis, and Graves. The following prophylactic measures are suggested to lessen the tendency of trauma producing cystocele:

1. Proper management of labor to insure a normal mechanism, avoid too rapid deliveries and injudicious instrumental applications, resort more frequently to episiotomy.

off the internal sphincter, does not depress with the trigone. In other words, when the patient strains, there may be even a definite urethral obstruction, first, in spasm of the internal sphincter, and second, in that the latter is relatively raised from the floor of the bladder. It is to correct this last defect in particular, that this operation is devised. As the operation probably does not actually unite the severed ends of the trigone muscle, but approximates them enough to function, some individuals may occasionally require subjective relief by urethral dilatation after operation. Such dilatation would be the exception

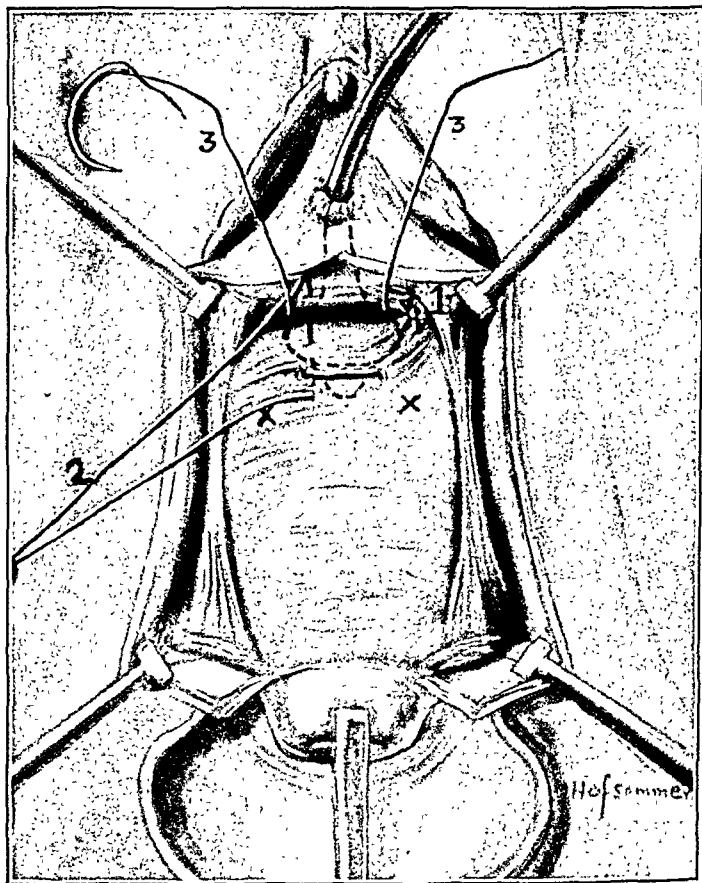


Fig. 5.—Traction on mushroom catheter marks site of internal sphincter just anterior to bulbous tip. X marks the location of the ureteral orifices. 1, Anteroposterior suture tied. 2, Similar suture on opposite side placed from a point three-fourths of an inch anterior to and carried to a point three-fourths of an inch posterior to the internal sphincter. 3, Mattress suture placed for reinforcement at the internal sphincter. Catheter is removed before any sutures are tied.

and it might well, in a few instances, be supplemented by cystoscopic diathermy of any urethral tabs which could initiate the spasm and thus cause symptoms.

This type of injury is very frequently associated with urethrocele due to internal sphincter damage, but is a distinct clinical entity.

OPERATION

Under morphine-hyoscine and local infiltration with one-fourth of 1 per cent of novocaine to which is added four minims of 1-1,000 adrenalin per ounce, an inverted

2. In cases of partial injury to the trigonal muscle, with release and consequent spasm of the internal sphincter, urethral dilatation to the point of tolerance is advisable during the early puerperium.

Routine cystoscopic examination, prior to all cystocele repair operations, is advised as a diagnostic aid in order to determine the location and extent of the injury. With the bladder filling slowly and not too full, have the patient strain, and through the cystoscope note:

1. Whether the sphincter depresses promptly and directly with the contractions of the trigone muscle when the patient tries to void.
2. If any cystocele is present, and if it is above or below Mercier's bar.
3. The presence and location of any true or pseudodiverticula.
4. The presence of trabeculae (hypertrophied muscle in the bladder wall) in early cases, and the thin, atrophic bladders in those of long standing.
5. The presence or absence of a relaxed or spastic internal sphincter.

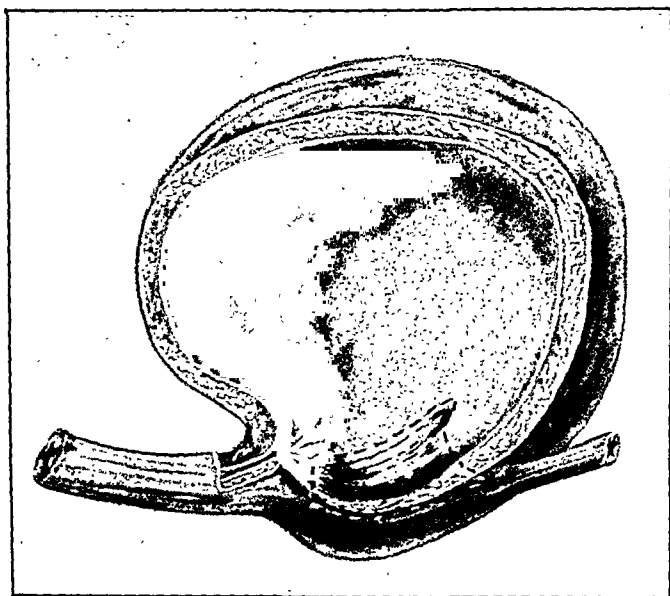


Fig. 4.—Diagrammatic representation of point of injury anterior to Mercier's bar where the urethra is sheared from the trigonal muscle near the internal sphincter. Note abnormal curve of urethra, due to elevation of the internal sphincter. (Modified after Kelly and Burnam.)

6. At the height of a bladder contraction, note the distance from the internal sphincter to the floor of the trigone.

7. The presence or absence of any contracting torn ends of the trigonal muscle.

The damaged internal sphincter is a prime cause of urinary incontinence. If the cystocele is anterior to Mercier's bar, the result will depend upon the ability of the remaining trigone muscle fibers to compensate and perform the function intended for the whole; hence, when such injury is present, early repair, before loss of bladder tone, offers the best hope of cure.

In many instances of the particular type under discussion, there will be very little external evidence of cystocele. However, on cystoscopic examination, with the patient straining, the urethra, being sheared

base of the trigone muscle. These sutures restore the normal axis of the urethra. A deep mattress suture then reinforces the internal sphincter and fixes it to the trigonal muscle. The mushroom catheter is removed before any sutures are tied. A running lock-stitch of fine chromic catgut then plicates the fascia from a point near the meatus all the way back to the corpus uteri to which the fascia is elevated and fixed as high as possible. A second running lock-stitch (or half lock-stitch), using No. 1 chromic catgut, then reinforces this fascial attachment, avoiding undue tension. The bases of the broad ligaments are sutured anterior to the cervix to elevate same, and the vaginal wall is approximated with a continuous lock-stitch of No. 1 chromic catgut, after excising any redundant tissue, taking care to leave ample flaps for approximation. In cases of vaginal hysterectomy, the cardinal supporting ligaments of the uterus are plicated beneath the bladder in the customary manner. A perineorrhaphy is usually done after completion of the anterior colporrhaphy. This repair elevates the cervix, bladder floor, and urethra. It enables the patient to empty her bladder without undue strain. It is an attempt to restore anatomic relations of the trigone so as to permit satisfactory function. Thus far, we have done six operations by this method, five of which have functioned satisfactorily. The sixth patient was improved; though failure to carry the repair suf-

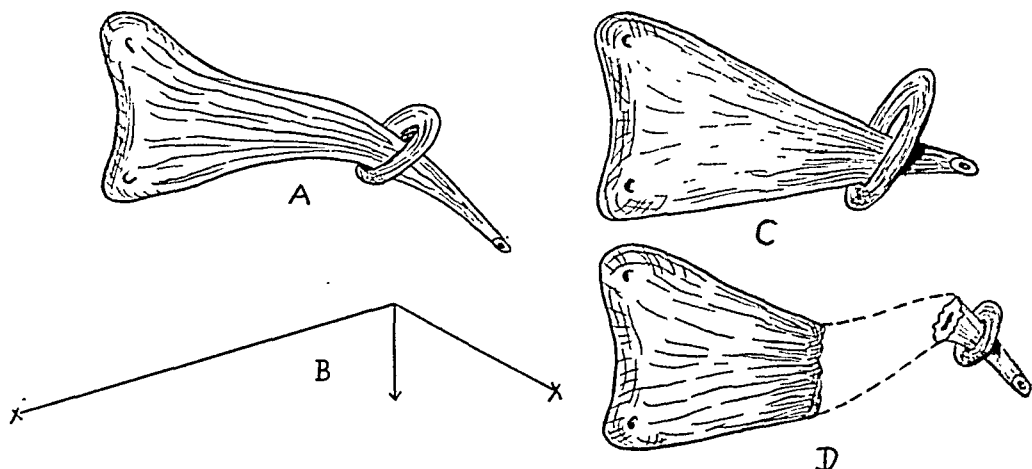


Fig. 7.—Schematic modification after Van Duzen, from Young's *Urology*. *A* shows the normal trigonal muscle passing through internal sphincter. It is fastened in the floor of the urethra. *B* shows angle of traction during voiding. *C* shows trigonal muscle, thicker and shorter in contraction, opening the internal sphincter. *D* shows trigonal muscle severed at or near internal sphincter.

ficiently far anteriorly to the internal sphincter did not give complete relief from urinary frequency, because of imperfectly fixing the urethra to the trigone. It is suggested as a method of repair in cases where satisfactory results have not been obtained up to the present time.

SUMMARY

This operation is devised for the specific type of cystocele described, where methods of repair thus far have been unsatisfactory. This correction lies in splinting the entire urethra, excepting the anterior 1 cm., by means of a running catgut stitch, which continues past and through the lower segment of the internal orifice to a point posterior to the midtrigonal region.

This suture, besides uniting and splinting the urethra to the trigone, pulls down the anterior urethra and meatus and fixes the internal

T-incision is made through the anterior vaginal wall from the cervix to a point within 1 cm. of the meatus. A large volume of infiltrating fluid facilitates dissection of the vaginal flap from the bladder. The nearer one approaches the meatus; the more difficult is the dissection. Great care must be taken to avoid injury to the urethra. The bladder is freed from the uterus by blunt dissection almost as high as its peritoneal reflexion. The incision near the cervical tip is carried bilaterally far enough to expose the bases of the broad ligaments. A number eighteen French, mushroom tip catheter is inserted into the bladder, and traction on the catheter marks the site of the internal sphincter, just in front of the bulbous tip, making due allowance for any marked urethrocele. A fine catgut suture, preferably 00 or 000 chromic, on a fine curved intestinal needle, takes a deep bite anteroposteriorly

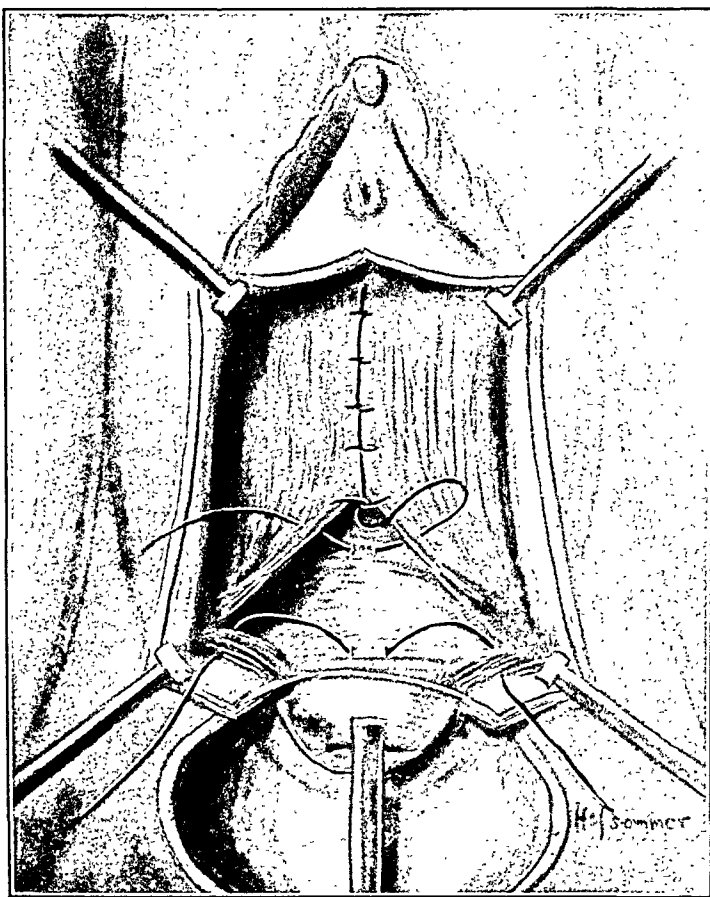


Fig. 6.—Plication of fascia with fine chromic catgut beginning as near the meatus as dissection has made visible and carried posteriorly to the corpus uteri to which it is fixed, advancing the bladder to a higher level. Bases of broad ligaments are sutured in front of the cervix which is elevated.

in the tissue close to the side of the urethra, three-fourths of an inch or more, in front of the internal sphincter, and is carried in the vaginal axis, intermittently, through the outer thickness of the bladder wall posteriorly to a point three-fourths of an inch behind the internal sphincter, not crossing the midline of the body. Emphasis is placed on carrying the suture anteriorly to a point within 1 cm. of the meatus. The suture should not be carried high enough posteriorly to obstruct the ureter, which is normally 3 cm. behind the internal sphincter. The two ends of this suture are not tied until a similar suture is placed on the opposite side of the urethra, thus fixing both sides of the trigone muscle to the urethra anteriorly to the internal sphincter. When the cystocele is marked, a third such suture may be placed in the midline, from beneath the urethral wall to a point well back on the

SIGNS AND SYMPTOMS

The classical textbook description of these cases mentions that there is usually a background of toxemia; that the lesion develops in the last trimester of pregnancy, and is characterized by the sudden onset of a small amount of bleeding out of all proportion to the accompanying constitutional signs of shock. Indeed there may be no bleeding evident at any time, hence the appellation, concealed hemorrhage. With or without bleeding, there is the sudden development of uterine pain and tenderness, accompanied by uterine rigidity of such a nature as to give a woody or doughy feeling on palpation. There may be even some generalized abdominal rigidity and tenderness if the lesion is sufficiently gross. There are increased or agonal fetal movements, which end in the death of the fetus if the placenta separates sufficiently, or separates near the cord insertion. In any case there is usually evidence of some sort of dire fetal distress. The outstanding aspect of the picture, perhaps, is the generalized shock. As it resembles surgical shock from other causes, there is no need to enumerate its details here.

The termination of such a case may vary. Either the hemorrhage is profuse and intractable and the woman dies, or the hemorrhage may be scarcely revealed but be extensive internally and have the same termination; or the placenta may separate completely, the fetus die, the lesion become quiescent, and a "missed abortion" be carried for a time until labor sets in and the macerated fetus and placenta are expelled. On the other hand the lesion may be small, only a little of the placenta may separate; then for some reason the whole process subsides, may or may not recur, and the pregnancy goes to term or to near term, a live baby is delivered, and the placenta displays one or more large or small marginal infarcts or organized clots.

We do not feel, however, that the true picture of all cases of abruptio placentae is adequately represented by the foregoing description. In a previous paper³ it was pointed out that just as a pregnant woman showing polyneuritis and icterus after prolonged hyperemesis can scarcely be said to represent completely the classical evidences of hyperemesis gravidarum, in the same way such severe cases as the texts describe do not represent the entire group of cases which should be labeled abruptio placentae. Myxedema is not the typical and exclusive picture of hypothyroidism. Until we come to a more typical and accurate clinical description of abruptio, we shall fail to recognize early cases and be unable to administer prophylactic therapy. We will be forced to fall back upon the pessimistic view expressed recently by Baird in his review of ten years' experience at the Glasgow Maternity. He concluded "antenatal care can do little in the prevention of accidental hemorrhage."

In the course of a detailed study of the problem of the premature interruption of pregnancy, the details of which have been published else-

orifice to the line of suture. In addition to the splinting suture described, are those sutures placed parallel to the long axis of the urethra which, besides supplementing the effects of the running urethral trigonal lock-stitch, also bunch tissues at the internal orifice. This latter bunching effect in turn is supplemented by a mattress suture overlapping the fascia.

This functional bladder repair may be incorporated, in suitable cases, in any standard operation for repair of cystocele.

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THE EARLY DIAGNOSIS OF ABRUPTIO PLACENTAE AND ITS TREATMENT WITH WHEAT GERM OIL

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ABRUPTIO placenta under one or other of its numerous names has been a well-recognized entity for many years. It has been variously referred to as accidental hemorrhage, concealed hemorrhage, ablatio placenta, and premature separation of the placenta. The lesion thus referred to is really a premature, and usually partial, separation of the placenta which lies on the fundus or sides of the uterus but not in the position we describe as previa.

INCIDENCE

The incidence of this condition is variously given by the different clinics and authorities. It ranges from 0.18 per cent (Kraul) to 1.06 per cent (Cragin, Goethals¹), or even 2.8 per cent (Baird²). Either there is a very great variation in its incidence in various parts of the world, or there is a variation of opinion as to what should be classified in this pathologic group. We believe the latter is the more likely explanation. Undoubtedly many cases of this type are overlooked, both in hospital and home practice, because placentas are not examined routinely and minutely by competent obstetric pathologists. Moreover there is lacking in the literature an adequate description of the signs and symptoms which characterize early or mild degrees of abruptio placenta. As a result, only the most startling and striking cases are ever recognized as such.

undoubted evidences of much recent organized blood clot at its margin might be expelled by a woman who could not remember anything one might link up with such a diagnosis.

We observed cases of the type we have described more frequently in the late winter and spring than at any other time of year. They were least frequently encountered in the late summer and early autumn.

SEROLOGIC STUDIES

As was mentioned, we were engaged in a study of all types of cases of premature interruption of pregnancy, and this group of cases bulked large in such a series. It occurred to us, therefore, to test their blood serums for evidence of the imbalance between vitamin E and estrogenic substance which characterizes most women who are aborting or miscarrying spontaneously. We have developed a simple laboratory test⁴ in order to disclose vitamin E deficiency or excess of estrogenic substance in the blood and, accordingly, this was employed. We might add that certain uncompleted spectrophotometric studies of these serums, which we have carried out under the direction of Mr. G. A. Adams of the Department of Biochemistry, gave us no reason to think that vitamin C deficiency was present. Moreover, we have seen classical cases of abruptio develop in women whose C intake was unusually high.

Our results are tabulated here. In the first year of our investigation we paid very little attention to the cases of abruptio. As our interest was aroused, however, and a more sensitive test for E-deficiency was developed, we secured very interesting results. Evidences of vitamin E deficiency seemed to be intimately associated with the clinical signs and symptoms we have described. We excluded seven cases from consideration in which the test was done long after the placental detachment had been responsible for fetal death, because our test is useless very soon after complete placental detachment, whether normal or abnormal, has occurred.

DURATION OF EXPERIMENT	NUMBER OF CASES	PERCENTAGE SHOWING A RELATIVE DEFICIENCY OF VITAMIN E AND THEREFORE AN EXCESS OF BLOOD ESTROGENIC SUBSTANCE
Jan. 1, 1934—Jan. 31, 1935	5 cases	80 per cent
Feb. 1, 1935—May 31, 1936	77 cases	78 per cent
29 months in all	82 cases	78 per cent

Of these 82 cases, only 31 were of the severe classical type described in standard works. Of these 31 severe cases, 81 per cent revealed vitamin E deficiency.

WHEAT GERM OIL THERAPY

In a series of 44 cases of spontaneous abortion we had found that 73 per cent showed evidences in the blood serum of deficiency of vitamin E.^{4, 6} It has now become generally recognized⁹⁻¹¹ that vitamin E has great prophylactic and therapeutic value in the treatment of abortion.

where,⁴⁻⁷ we came across a group of cases which we wish to present for consideration in this regard. At any time these cases might terminate in a typical abruptio with the classical signs and symptoms described above. We found these cases very numerous, indeed, and wondered if abruptio placentae could really be as frequent in a mild form as this would indicate. At about that time we came upon the study of Goodall,⁸ who in 750 placentas obtained from consecutive deliveries in Montreal, found that 600 bore evidence of some hemorrhagic lesion but that in only eleven instances had there been bleeding from the vagina during gestation.

The most frequently encountered and significant sign in these cases, by all odds, was the gradual appearance of a restricted, palm-sized area of true uterine tenderness, accompanied by steady sacral backache. Occasionally these features were soon followed by the occurrence of labor pains, violent fetal movements, and uterine hemorrhage of any grade of severity. Or a gradual elevation of blood pressure developed, accompanied by edema of the extremities, rapid gain of body weight and even albuminuria, indicating an early toxemia or pregnancy. The uterine tenderness in severe cases usually spread over the whole uterus or a large area of it. It might, however, disappear spontaneously, together with all the other signs or symptoms mentioned except the evidences of toxemia. If the latter once showed themselves they tended to persist and progress as is usual. When the same signs and symptoms of tenderness, pains, and hemorrhage recurred, as often happened, the area of tenderness was in the same location as before. In four instances we were able to determine that this area of tenderness coincided accurately with the placental site. These were cases of manual removal of the placenta at cesarean section or at the extraction of twins per vaginam.

When these women went on to miscarry or deliver at term, with or without treatment, the placentas were usually small for the duration of the gestation. Almost always they displayed one or several marginal lesions, ranging in character from fresh blood clot to recently organized, leached clots resembling cheese in consistency—or even appearing as white infarcts. These white infarcts might be 2 or 3 mm. deep on the maternal aspect of the placenta or might penetrate through the placental substance to the fetal side. The frequency of such placental lesions was quite comparable to that mentioned by Goodall. Women who expelled such damaged placentas could usually recall one or more slight or severe hemorrhages during gestation or perhaps a transient but definitely localized area of tenderness on the uterine wall. When this had disappeared and recurred, it had always recurred in the same location. However, placentas might be grossly normal in classical cases of abruptio placentae where there could be no doubt as to the clinical diagnosis. The reverse was also true, viz., that a placenta with

of salt-restriction, bed rest, or other standard measures. Some of these small fetuses seemed suddenly to increase in size in an amazing way. As we are well aware of the fallacy of estimating fetal size by abdominal palpation, we have recently begun to check this observation by more accurate roentgenologic means.

However, in women in whom the evidences of toxemia were of some duration, the beneficial results of the wheat germ oil therapy, at least as far as it concerned the signs of toxemia, were scarcely discernible. But such of these cases as displayed deficiency of vitamin E (or excess of estrogenic substance) in the blood serum did not go on to true eclampsia, in our limited experience, and with adequate vitamin E therapy could be safely induced when gestation was sufficiently advanced. The placentas adhered sufficiently well to enable induction and labor to proceed safely for mother and child.

DISCUSSION

Years ago Holmes¹² foreshadowed the division of the toxemias of late pregnancy into those which went on to eclampsia and those ending as ablatio placentae, as he called the lesion under discussion. There seems to be considerable justification for such a point of view. We see very few true eclampsia cases in this locality, but there have been eight such cases in the past three years whose blood serum we have tested for vitamin E deficiency and excess of estrogenic substance. Only one of the eight showed the defect in the particular hormone-vitamin balance just mentioned. Similarly Bickenbach and Fromme¹³ found no increase in the blood folliculin content in four eclamptic patients they observed. Indeed it would appear from the work of the Smiths¹⁴ that the blood and placentas of eclamptic patients are characterized by a low estrin and an excess of the antagonistic anterior pituitary gonadotropic hormone. Indeed, we have recently treated a convulsive eclamptic patient and a severe late preeclamptic patient by means of estrin with very suggestive and beneficial results.

Holmes,¹² Baird,² Davis and McGee,¹ and others have pointed out that abruptio placentae is only rarely associated with eclampsia or eclampsism. Le Lorier,¹⁵ for example, in 31 cases of hematomas retroplacentaires found only two associated with eclampsia. We suspect that the late toxemias of pregnancy may prove to be divisible into two main groups, those deficient in vitamin E and displaying an excess of estrogenic substance in the blood, and a very much smaller group with adequate vitamin E and characterized by an excessive excretion of prolactin. The former are cases in which abruptio placentae is actual or impending, the latter are cases in which true eclampsia is actual or impending. We have observed that those cases in which the excess of estrogenic substance was most marked were generally hypothyroid, and perhaps that feature of the endocrine picture of the toxemias should also receive notice. Hoffmann and Anselmino¹⁶ found that there was a great decrease of thyroid secretion below the normal for pregnancy in the blood of pregnant women showing renal damage, but that in eclampsia the content of thyroid secretion was much higher than the values for normal pregnancy.

It is quite understandable, therefore, that we began to study the corresponding use of a vitamin E preparation with which we were thoroughly familiar* in cases of abruptio placentae. Such an oil must be kept cold, and be not more than eight weeks old.

The results have been very encouraging, although it is too early yet to assess them properly. Obviously those patients first seen when placental detachment is already complete or nearly complete offer little excuse for anything but the classical measures used everywhere for such an emergency. We cannot but suspect, however, that a closer search for true uterine tenderness during pregnancy, combined with an early test of the blood serum for the presence of the specific hormone-vitamin imbalance we have described, would to a great degree prevent the occurrence of such severe cases.

It has been our experience with the less severe cases that, when properly and adequately saturated and kept saturated with vitamin E (as determined by clinical evidence and repeated tests of the serums), they have not progressed to a severe stage of placental detachment with death of the fetus. In approximately twenty hours, an adequate massive dose of eight to twelve drams of bulk wheat germ oil has completely abolished the characteristic circumscribed area of uterine tenderness. The accompanying severe sacral backache and uterine cramps have subsided as rapidly. When uterine hemorrhage has been present, it has responded promptly as well. Within the first day of treatment the patients have remarked that their indescribable subjective discomfort has disappeared. One patient who developed a Couvelaire apoplexy of the uterus described these sensations as resembling those of "a cold coming on." Stopping the oil therapy has often been followed by a recurrence of uterine tenderness and bleeding, which, in turn, have disappeared on further vitamin E therapy. No case recognized early and treated adequately has gone on to the severe classical type.

Our best results have been obtained in women who showed little or no evidence of an associated toxemia. We can say in passing, however, that where such toxemia was detected very early, at the first rise of blood pressure beyond the accepted critical level, at the first continued excessive gain of weight or appearance of edema, at the first mild albuminuria or in patients in whom by abdominal palpation the fetus seemed unusually small in consideration of the duration of gestation or was surrounded by some excess of amniotic fluid, wheat germ oil therapy was immediately beneficial. The blood pressures, both systolic and diastolic be it noted, returned to normal levels and were maintained there as long as the patient remained saturated with wheat germ oil. Albuminuria ceased. The unusual rate of weight gain was diminished, or the patient might even lose weight. Edema decreased, sometimes with frequency and polyuria, and all this without the use

*Viteol, supplied by the Canada Pharmacal Company, London, Ontario.

5. Wheat germ oil, therefore, was used prophylactically and therapeutically. The results were very satisfactory.

6. The relationship of this new evidence to the problem of the toxemias of late pregnancy is discussed.

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CYSTOGRAPHIC DIAGNOSIS OF PLACENTA PREVIA

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PLACENTA previa is associated with such a high mortality, both fetal and maternal, that even a suspicion of the condition leads to grave apprehension on the part of the attending obstetrician and often to too rapid a decision for cesarean section. Since the advent of the x-ray there have been innumerable attempts to use this procedure as an aid in the diagnosis.

Campbell and others in 1932 mentioned the possible use of strontium iodide as a means of diagnosing the position of the placenta in utero. Menees, Miller, and Holly in 1930 injected strontium iodide into the uterine cavity through the abdominal and uterine walls, thus making the amniotic fluid opaque to the roentgen rays. By this method the placenta could be outlined as a bulging mass or a filling defect into the cavity. They noted that in many of the cases labor was instigated and that premature delivery was the result. Snow and Powell¹ in 1934 report that Snow first recognized the placenta in a simple flat plate of the abdomen. They were able to demonstrate the position of the placenta and explained that the placenta causes an obstruction to the rays due to the greater density of the tissues and blood vessels that made up the placenta in contrast to the lesser consistency of the amniotic fluid. They also suggested the possibility of using this method as a possible means of diagnosing placenta previa. Ude, Weum and Urner² also in 1934 reported the positive diagnosis of three cases of placenta previa and one of premature separation of the placenta by the use of sodium iodide injected into the bladder followed by a cystogram. The placenta was demonstrated as a mass be-

In previous papers^{5, 6} we have expressed the belief that vitamin E in the pregnant woman acts by neutralizing estrogenic substance which, when present in excess, resists the intrusion of the placental villi into the uterine wall. We endeavored to explain in this way the fundamental mechanism of abortion, miscarriage, and premature labor. Perhaps the mechanism underlying the development of abruptio placentae is not dissimilar.

McGlinn and Harer¹⁷ have recently expressed this possibility in very thought-provoking words, "All writers stress traumatism, endometritis, diseases of the ovum, emotional states and toxæmia. It is quite possible that we must look to the early development of the placenta for the real underlying cause. This embryologic factor may quite possibly be a paucity of anchoring villi, so that the placenta is from the very beginning only loosely attached to the decidua basalis. Such a placenta, particularly when subjected to the additional pathologic changes that so frequently accompany late gestational toxæmia, would naturally be expected to separate from its uterine attachment—unquestionably, a placenta that is the site of large infarcts is less firmly attached to the decidua than is a normal noninfarcted placenta."

Many interesting avenues for further investigation are opened up by this study. It offers a further aid in the differentiation of abruptio placentae and placenta previa. Theobald¹⁹ has expressed the belief that all the toxemias of pregnancy may prove to be interrelated and due to dietetic deficiencies. This may be as true for the group of abruptio cases as for the neuritis cases with which he has been engaged.

New insight into the problem of nephritis, as associated with pregnancy at least, and all its related pathologic phenomena may also develop from it. Interesting possibilities of antagonisms and synergisms existing between the hormones and vitamins present themselves. With such antagonisms as exist between estrin and progestin or estrin and anterior pituitary gonadotropic hormone, or such synergism as that existing between estrin and postpituitary oxytocic hormone, we are already familiar. Collip¹⁹ and others have suggested the presence of anti-hormones for hormones other than estrin.²⁰ It is known that vitamin D is estrogenic. But this picture of an equilibrium existing between estrogenic substance and vitamin E is not quite identical with any such relationship as has been mentioned.

SUMMARY

1. Many cases of abruptio placentae are overlooked because the early symptoms are not recognized.
2. The early symptoms are described in detail, stressing localized uterine tenderness and sacral backache.
3. The marginal retroplacental hemorrhages and clots are described briefly.
4. Seventy-eight per cent of 82 cases of mild and severe abruptio placentae showed serologic evidences of deficiency of vitamin E.

bladder and an associated suspicious history led us to consider the patient to have a complete or central placenta previa (Fig. 4). It must be borne in mind that the presence of blood clots from a premature separation, which have settled into the lower uterine cavity, is capable of giving a similar picture, either of the marginal or central type. In either event the condition would in all probability be abnormal. In all doubtful cases the plates were either repeated or the patient observed until she showed more definite signs of the condition.

In our cases we observed that the cystogram was satisfactory only during the last trimester of the pregnancy, due to the fact that in earlier pregnancies the head was still floating above the brim of the pelvis with the result that there was no pressure being made on the bladder. It is better to have the patient in the early first stage of labor or at least have the head below the brim. In the presence of prematurity the fetal head is not large enough to entirely fill the pelvis, with resulting unsatisfactory pictures. The entire diagnosis depends upon the ability of the fetal head to exert pressure downward onto the bladder. The amniotic fluid, acting as a transmitting agent, will then give the desired pressure on the urinary bladder, causing the even concavity of its upper border.

CASE REPORTS

CASE 1.—Mrs. M. B., aged twenty-one, para 0, gravida i, was first seen in the prenatal clinic on Mar. 25, 1935. Last menstrual period was in November, 1934. Physical examination at the first clinic visit was essentially negative. Pelvic measurements adequate. Prenatal period uneventful except for "hematuria" on Apr. 29, 1935. Patient was admitted to the hospital on July 19 with a history of having painless vaginal bleeding on July 18, similar to normal menstruation. Membranes were intact on admission. Some complaint of aching low in the back and right side. Physical examination negative. The abdomen was the size of a full-term pregnancy, head not engaged, and the fetal heart tones well heard in the left lower quadrant. On the day after admission the bleeding had checked but there was still some cramplike pain in the abdomen. She had no more bleeding or pain and on July 24 a cystogram was done with a diagnosis of probable placenta previa (Fig. 1). Laparotrachelotomy was done on July 26 and a living child delivered, which died about six and one-half hours after delivery. (Autopsy on the baby revealed bilateral congenital atelectasis.) The placenta was found to be laterally placed. Convalescence of the mother was uneventful and she was discharged on August 4.

CASE 2.—Mrs. R. L., aged twenty-six, para i, gravida ii, admitted to the hospital on July 24, 1935, with a history of rupture of the membranes on July 19 and the onset of uterine bleeding on July 23. General physical examination was essentially negative. The fundus uteri extended to two fingers above the umbilicus with the fetal heart tones heard in the left lower quadrant. A cystogram was done soon after admission but was unsatisfactory due to the prematurity of the fetus. She was observed for three days, went into labor on July 27 and delivered a living premature child that day. The placenta was normally placed. Puerperium uneventful.

tween the fetal head and the upper concave border of the bladder. They made the note that the procedure was not satisfactory in cases of breech or transverse presentation. In 1935 Ude and Urner³ studied all cases of abnormal bleeding that came to their attention and reported fourteen positive cases of placenta previa as diagnosed by the cystographic method. All of their cases were confirmed at operation with the exception of one in which there was no note made as to the position of the placenta. They also made a study of normal cases on which to base their diagnosis of abnormal position of the placenta. They found that in the full-term pregnant woman there is a distance of approximately 1 cm. between the upper concavity of the bladder and the lower convexity of the fetal head as it descends into the pelvic canal (Fig. 2). The demonstration of a mass between the head and the bladder constituted their diagnosis of either a previa or a blood clot when the clinical manifestations were suggestive of some pathology.

The scope of this paper is to present nine cases of abnormal uterine bleeding during the last trimester of pregnancy in which the diagnosis of placenta previa was made in seven as a result of cystographic examination. In the seven cases cesarean section was elected as the method of delivery of choice.

TECHNIC OF THE CYSTOGRAM

A cystogram was done on all patients who were admitted with a history of abnormal bleeding during the latter months of pregnancy, or who came to the hospital not necessarily in labor but because of bleeding. The patient was first catheterized to empty the bladder completely. We then used the technic as outlined by Ude and Urner with few minor variations. From 30 to 40 c.c. of an opaque material, usually 12½ per cent sodium iodide, was then injected into the bladder and the catheter removed. A flat plate of the lower abdomen with the patient in the supine position was then made. An effort was made to prevent a tilting of either the table or the tube thus permitting the rays to pass straight downward. The first plate was then immediately developed and read. If there was too much material in the bladder, as evidenced by an "overlapping" of the upper border, from 10 to 15 c.c. was removed and a second plate made. A large enough film was used to permit exposure of the entire pelvis and approximately half of the fetus.

CRITERION OF DIAGNOSIS

As noted by Ude and Urner there is normally a distance of about 1 cm. between the fetal head and the upper margin of the bladder. This distance should be the same across the entire top of the bladder. In the majority of our cases where a positive diagnosis of previa was made there was usually on one side the expected 1 cm. (more or less) with a gradual or sudden widening out as the opposite side was approached, until a distance of sometimes 3 or 4 cm. was obtained (Figs. 1 and 3). We considered this as suggestive of marginal placenta previa. A separation of from 2 to even 4 cm. across the entire upper margin of the

CASE 4.—Mrs. A. P., aged twenty, para 0, gravida i, clinic patient with an uneventful prenatal period until Sept. 14, 1935, when she began having a slight amount of painless uterine bleeding. Admitted to the hospital on September 16. Membranes intact. Physical examination negative. Fundus three fingers above the umbilicus with the fetal head at the pelvic brim. Fetal heart tones in the left lower quadrant. Position left occiput anterior. Cystogram done soon after admission which was negative for previa (Fig. 2). Bleeding did not recur and she was discharged on September 18. Readmitted on September 26 and discharged again as not in labor on October 1. Readmitted for the third time on October 18 and delivered a normal full-term living child on October 19 with low forceps. Placenta was normally placed. Discharged after an uneventful puerperium on October 22.

CASE 5.—Mrs. R. S., aged twenty-nine, para i, gravida ii, was not a prenatal clinic patient. She was first admitted to the hospital on Aug. 26, 1935, with a history of uterine bleeding. A cystogram which was doubtful, due to the prematurity of the fetus, was made on August 27. She was discharged from the hospital and was readmitted on September 23 with a history of having had one attack of bleeding during her interval at home. On September 23 she had been awakened

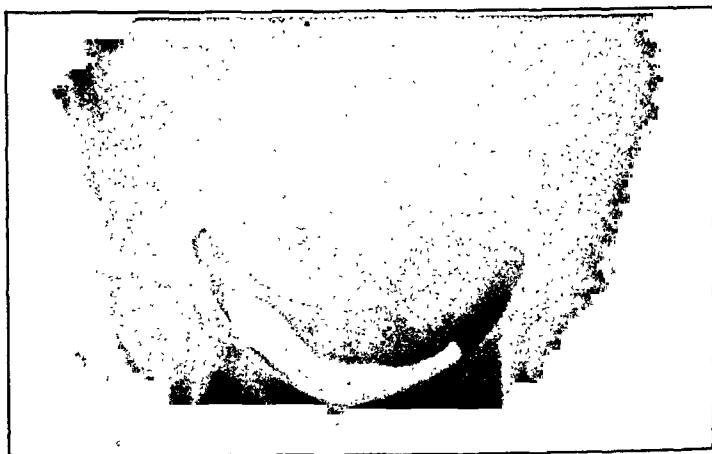


Fig. 3.—Mrs. R. S., aged twenty-nine, para i, gravida ii. There is a definite increase in the separation of the fetal head and the bladder beginning at about the midline and gradually increasing toward the left side. A diagnosis of left lateral placenta was made and confirmed.

from sleep to find that she had bled enough to saturate her bedclothing. She came immediately to the hospital and was still bleeding on admission. Physical examination revealed her to be in low-grade shock with a blood pressure of 55/40. Hemoglobin 30 per cent. The fundus uteri was halfway between the umbilicus and xiphoid. There were no uterine contractions. Immediate transfusion of 500 c.c. citrated blood given along with routine shock treatment. Reaction was good and about twelve hours after admission the blood pressure had risen to 100/60. Cystogram was done as soon as it was possible to move the patient and a diagnosis of probable placenta previa was made (Fig. 3). Low cesarean section was done under local anesthesia and a living premature child was delivered, which died about twelve hours after delivery. The placenta was definitely laterally placed. Convalescence of the mother was uneventful except for a postoperative bronchitis which cleared up without difficulty. She was discharged on October 4 to the care of her private physician.

CASE 6.—Mrs. R. S., aged twenty-five, para i, gravida ii. Last menstrual period on Dec. 18, 1934. First seen in the prenatal clinic on July 23, 1935. Pelvic measurements were adequate. She was admitted to the hospital on September 24

CASE 3.—P. T., aged forty, para vi, gravida vii. Last menstrual period was Dec. 5, 1934. First seen in the prenatal clinic on June 12, 1935. Physical examination at that time was negative. Pelvic measurements adequate. Admitted to the hospital on August 10 with a history of profuse painless bleeding early that morning. Membranes intact. General physical examination was negative. Fundus was about the size of a full-term pregnancy, with the fetal heart tones well heard in the left lower quadrant. Position left occiput anterior. Cystogram done on August 10 and a diagnosis of partial or central placenta previa made. Cesarean section



Fig. 1.—Mrs. M. B., aged twenty-one, para 0, gravida i. Cystographic findings similar to those in Fig. 2 but which are not as well defined. There is a gradual increase in the separation beginning about 3 cm. from the left border of the bladder toward the right. A positive diagnosis of right lateral placenta previa was made

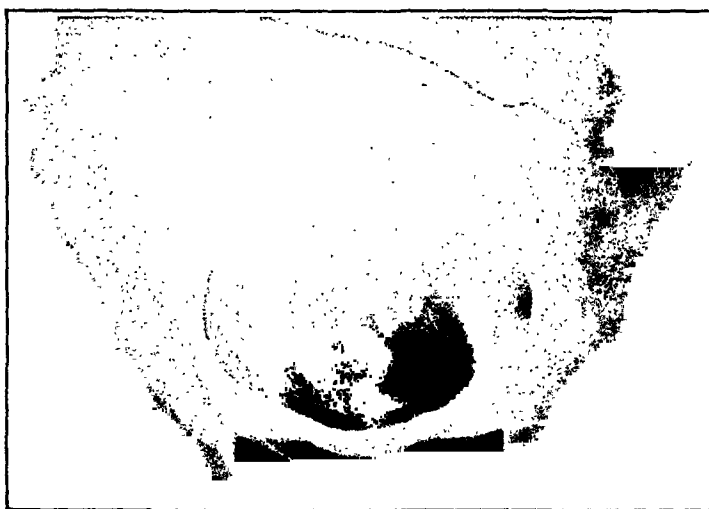


Fig. 2.—Mrs. A. P., aged twenty, para 0, gravida i, admitted with history of painless uterine bleeding. Cystographic findings illustrated that there was a constant distance between the fetal head and the upper concavity of the urinary bladder. At delivery the placenta was found to be normally placed.

done on August 10 and a living child obtained. The placenta was partially occluding the internal os. Convalescence of the mother was very satisfactory until the ninth postoperative day when she began complaining of pain in the left chest. She subsequently developed an abscess in the left upper lobe of the lung which was drained by the two stage thoracoplasty method. Discharged from the hospital as healed on Nov. 19, 1935.

mitted to the hospital, and was treated with opiates, rest, etc. The bleeding checked and she was discharged after two days. She remained in bed at home for one week. On December 30 she had a sudden large hemorrhage followed by slight bleeding daily until Jan. 3, 1936, when she again had a sudden gush of blood followed by laborlike pains which lasted eight hours. She had had no pains for twelve to fourteen hours before admission. On admission physical examination was negative. Blood pressure 124/84. Fundus was at the xiphoid. Vertex presentation. Position right occiput anterior. Fetal heart tones high on the right. There were blood clots in the vagina. Hemoglobin 58 per cent. Cystogram was made and a diagnosis of placenta previa was suggested even though the head was high. She was observed until January 6 when she was given a transfusion of 550 c.c. of citrated blood. Laparotrachelotomy was done two hours after the transfusion, and a full-term living child was delivered. Placenta was found to be lateral in type. Convalescence uneventful. Discharged on January 16.

CASE 9.—E. L., aged twenty-two, para i, gravida ii. Last menstrual period on May 6, 1935. First seen in the prenatal clinic on Sept. 27, 1935, at which time the fundus was 17 cm. above the top of the symphysis. Fetal heart tones were not heard. There was slight vaginal bleeding at that time. Two weeks later, after rest in bed, vaginal spotting was still present. The fetal heart tones were present in the left lower quadrant of the abdomen. Placenta previa was suggested as a possible cause of the bleeding. Patient continued spotting intermittently until October 19. On December 20 the placental souffle was definitely heard over the right inguinal region. She was admitted to the hospital on December 29 and a cystogram made on December 30—head too high for accurate diagnosis. Discharged on Jan. 3, 1936. Readmitted on February 6 with a history of slight bleeding on one occasion since her previous admission. On examination there was some hyperemia of the nasal mucosa with a few crackling râles at the left base. Blood pressure 110/78. Fundus uteri two fingers below the xiphoid. Head floating over the pelvic brim. Fetal heart tones in the left lower quadrant. Position left occiput anterior. No labor pains. Cystogram was repeated on February 8 and a diagnosis of placenta previa was made. Laparotrachelotomy was done on February 9 under local and gas anesthesia with delivery of a living child. Placenta was partially occluding the uterine os. Convalescence was satisfactory except for a slight wound infection at the upper angle of the incision. Discharged on February 22.

In this series of nine cases a positive diagnosis of placenta previa was made in seven. The policy of the attending staff of the hospital has recently been to deliver patients of this type by cesarean section, which has given excellent opportunity to study and confirm the cystographic findings. In all of the patients who were delivered by section, the placenta was found to be either partially or completely occluding the internal uterine os. However, it is not intended here to discuss the treatment of placenta previa, but rather its diagnosis. We feel that any procedure that leads to a more correct diagnosis is valuable regardless of the method of delivery of that case.

Needless to say there have been equally as many patients with abnormal bleeding during the last trimester of pregnancy in which the diagnosis of placenta previa has not been made cystographically. These patients have been treated conservatively and subsequently delivered without difficulty. When the classical symptoms and physical findings of placenta previa are present and there is the added suggestion of the

with a history of bleeding without labor pains for seven to ten days before admission. Flow was similar to that of a normal menstruation. On September 23 she passed "something" described as a part of the placenta by a local physician. Membranes were intact. No labor pains. Physical examination was negative. Fundus was three fingers below the xiphoid. Fetal head was above the pelvic brim. Fetal heart tones were in the right lower quadrant. Position right occiput anterior. The placental souffle could be auscultated just above the left inguinal ligament. The uterus felt rigid in spite of the fact that the patient complained of no pain. Cystogram was done soon after admission and was diagnosed as placenta previa (Fig. 4). Laparotrachelotomy was done on September 25 under local and nitrous oxide anesthesia, with delivery of a living child. Placenta was found to be central in type occluding the internal os. Convalescence of the mother was satisfactory. She was discharged on October 4.

CASE 7.—J. M. D., aged twenty-seven, para iv, gravida ix. Last menstrual period on Jan. 27, 1935. First clinic visit on Sept. 6, 1935. Pelvic measurements adequate. Prenatal period uneventful, except for some edema of the feet and slight visual disturbances, until October 13 when she began having uterine bleeding. She stated



FIG. 4.—Mrs. R. S., aged twenty-five, para i, gravida ii. The separation of the bladder and the fetal head is approximately the same across the entire top of the bladder. However, the measurement ranges from 3 to 4 cm. as contrasted to that of the normal of 1 to 2 cm. With the history and physical findings coordinating with the cystogram, a diagnosis of central placenta previa was made.

that she was asleep and was awakened to find she had soaked her bed. Bleeding continued intermittently until October 18 when she came to the clinic. Cystogram was made before admission to the hospital and was suggestive of placenta previa. On admission her physical examination was negative except for a slight edema of the feet. Blood pressure 126/76. Fundus was three fingers above the umbilicus. Head engaged in the pelvis. Fetal heart tones in the right lower quadrant. Position right occiput anterior. The placental souffle was heard in both flanks over the inguinal regions, but was greater on the left. Laparotrachelotomy under gas anesthesia on October 18 and an eight months' child delivered. The placenta was found to be partially occluding the internal os. Postoperative convalescence uneventful. Discharged on October 26.

CASE 8.—I. H., aged thirty-six, para iv, gravida v. Last menstrual period on May 4, 1935. First seen in the prenatal clinic on Oct. 14, 1935. Original examination at the clinic was negative. Pelvic measurements adequate. Prenatal period uneventful until Dec. 3, 1935, when she had slight vaginal bleeding. She was ad-

BLOOD PHOSPHATASE IN PREGNANCY.

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THE special needs of the maternal organism in pregnancy have been recognized for a long time. It has been realized that the developing fetus imposes definite dietary requirements upon the mother. If these dietary constituents are not adequately supplied, deficiency states in either the mother or fetus, or both, may result. Support for this belief has been found in the altered chemical findings of the blood in the parturient woman, upon balance experiments in the latter months of gestation and from animal experimentations.¹⁻⁶ As a result many physicians routinely alter the diet of the mother, and especially increase her intake of the mineral constituents, particularly calcium and phosphorus. The occurrence of rickets in the newborn and in infancy is believed by a few investigators to be due in some instances to a deficient diet in the mother. In the past, cases of intrauterine rickets have been reported.^{7, 8} Rickets in the newborn and shortly after birth is not uncommon.^{9, 10} By the administration to the mother of an adequate mineral diet and a sufficient quantity of vitamin D some clinicians have observed an improved state of general health in the parturient woman and an absence of evidence of rickets in the newborn.⁵

During pregnancy and lactation the problem is therefore twofold: (1) maintenance of the health of the mother and (2) the maintenance of optimal conditions for the development of the fetus. The mother during pregnancy supplies all the substances necessary for the growth of the fetus. These substances the mother either obtains in her diet, synthesizes from her diet, or supplies to the fetus by depletion from her own tissues. If the maternal diet is deficient, this depletion may result in varying degrees of ill health of the mother, and, ultimately, of the fetus. Some of the commoner deficiencies in the maternal diet during pregnancy appear to be in vitamins A and D, calcium, phosphorus, iron, and iodine. An abundance of both vitamin D and calcium is essential for the proper development of the bony skeleton and teeth of the growing fetus. The maternal stores of vitamin D are small.¹¹ Her bones, however, constitute a large depot of calcium and phosphorus. These substances she can transfer to the developing fetus. If the maternal diet is deficient in calcium and phosphorus, the drain may result in osteomalacia, or, more commonly, dental caries in the mother.^{7, 11, 12}

condition found on x-ray, there should be no hesitancy in making the diagnosis. Conversely, if there are symptoms of previa which are not confirmed by the cystogram, observation of the patient can usually be made without as grave apprehension as usually accompanies hemorrhage.

SUMMARY

1. The technic of the cystogram is given and the criterion of diagnosis of placenta previa.

2. Presentation of nine cases which were studied as suspected placenta previa and in which the positive diagnosis was made in seven of the cases by use of the cystogram.

3. The delivery findings in the seven cases confirmed the diagnosis of either a lateral or complete placenta previa.

4. There was no maternal mortality.

5. Two of the children died after delivery, one from prematurity and the other from bilateral atelectasis.

6. The method of cystographic diagnosis is not suggested as an infallible one, but rather is to be used in conjunction with the history and suggestive physical findings of placenta previa.

Expression of appreciation is made to Dr. Karl Kesmodel and Dr. J. A. Meadows of the radiological staff of the Hillman Hospital for their kind assistance in the study of the x-ray plates.

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Lenner, A.: Hematoma of the Rectus Muscle in Women, *Acta obst. et gynec. Scandinav.* 15: 45, 1936.

Lenner reports two cases of hematoma of the rectus muscle in women. In the first patient a diagnosis of fibroid uterus had been made and in the second the diagnosis made was infected ectopic pregnancy. Both women had hemorrhages in the rectus muscles. A review of the literature revealed 72 cases of hematoma of the rectus muscle in women. Of these, 15 occurred in connection with pregnancy or labor and 57 in nonpregnant women. In the nonpregnant individuals severe coughing seemed to play an important rôle, especially in elderly women. In most instances, the hemorrhage was located in the right lower quadrant. The correct diagnosis was seldom made. Of the 15 cases occurring during the pregnant state, 11 occurred during the latter part of gestation, and in four the hemorrhage took place during labor or the early puerperium. The prognosis is favorable. In mild cases conservatism gives satisfactory results, but in serious cases an operation must be performed.

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Subbarow. At the same time the initial phosphorus content of the plasma is determined using another 2 c.c. of the original blood plasma. Both of these values are determined in mg./100 c.c. of blood plasma. The difference between these two values represents the number of milligrams of inorganic phosphorus liberated by the enzyme, phosphatase, from the substrate under the above conditions. Each milligram thus obtained is expressed as units of phosphatase per 100 c.c. of blood plasma. According to this technic we have found the normal values for adults to range up to 6 units, while for children values up to 15 units are to be considered normal.

TABLE I. PLASMA PHOSPHATASE IN PREGNANCY

Table showing the range and average values of plasma phosphatase, and average blood calcium and phosphorus values found in 201 cases of pregnancy. *Studies done during active labor. **Per 100 c.c. blood plasma.

Month of Gestation	3rd	4th	5th	6th	7th	8th	9th	Before*	Cord Blood	Days post-partum		
										1 to 3	4 to 6	7 to 10
No. of estimations	13	9	32	33	47	62	57	35	15	18	19	17
Units of phosphatase - Average**	2.03	2.45	3.02	3.36	4.79	8.33	10.35	12.53	4.01	10.09	8.33	6.90
Range in units of phosphatase**	1.64 to 3.04	1.23 to 3.90	1.30 to 4.44	1.40 to 4.48	2.16 to 8.58	2.40 to 17.80	5.66 to 24.48	5.98 to 22.60	1.84 to 6.64	8.48 to 17.04	3.16 to 13.44	3.64 to 12.64
Blood phosphorus Average-mg./100 cc. blood plasma	3.33	2.82	3.14	3.10	3.09	3.12	3.07	3.15	5.00	3.83	3.76	3.91
Blood calcium Average-mg./100 cc. blood plasma	18 cases - 11.50 mg.				44 cases - 10.44 mg.				7 cases - 10.60 mg.	12 cases - 11.19 mg.		
Graphic presentation of average phosphatase values	13 units											
	12 "											
	11 "											
	10 "											
	9 "											
	8 "											
	7 "											
	6 "											
	5 "											
	4 "											
	3 "											
	2 "											
	1 "											

As we have stated before, believing that the determination of this enzyme in the blood might prove to be a sensitive and early indicator of dysfunction of maternal or fetal bone metabolism, we have made plasma phosphatase determinations in a series of 201 parturient women in the various months of pregnancy. The results are shown in Tables I, II, and III. In all we have made 347 phosphatase determinations. In many instances we have repeated the determinations in the same individual during succeeding months of gestation. A few determinations in the first ten days following the delivery are also listed in Table I. We have in all instances done simultaneous blood phosphorus determinations and in many instances blood calciums. In passing it may be stated that we have noted no constant or suggestive relationship between the blood calcium and phosphorus estimations and the simultaneous blood phosphatase values. Mull and Bill²² have shown that in a series of pregnant

In recent years the study of the enzyme phosphatase has contributed considerably to our understanding of normal and pathologic bone formation.

This enzyme was first isolated by Robison in 1923 from ossifying cartilage.¹³ He believed at that time that the enzyme played a dominant rôle in the process of ossification. This view has been accepted by subsequent workers.^{14, 15} Numerous investigations have shown, moreover, that this enzyme is elevated in the blood above the normal in several groups of conditions, such as certain bone diseases,¹⁵ jaundice other than hemolytic,^{16, 17} and in many instances of malignant involvement of the liver.¹⁸ In bone disease it has found its greatest application in the study of Paget's disease and rickets.¹⁹ In rickets and in what is considered to be its adult equivalent, osteomalacia, the blood phosphatase is elevated in the active and progressive phases, and approaches normal as the disease state is brought under control. In rickets it is important to note that an apparent lag in the return of the blood phosphatase to normal during successful therapy is observed. Several recent writers on the subject feel that the blood phosphatase levels reflect more sensitively the status of bone metabolism in the body than does any other available test at the present time.^{15, 19}

In jaundice the phosphatase values have been found elevated in all forms except those of the hemolytic type. Some workers believe that the determination of this enzyme in the blood offers the best single means of differentiating between cases of obstructive and nonobstructive jaundice.^{16, 17} It has been suggested that the elevation in these cases of jaundice may be due to the altered carbohydrate metabolism accompanying the liver changes present, and that the elevation in these instances does not, therefore, reflect the same disordered bodily mechanism as is present in bone dyscrasias.²⁰

It has occurred to us that the study of the blood phosphatase levels in parturient women might provide some additional insight into the bone metabolism in pregnancy. Accordingly, blood phosphatase values were determined in a large series of pregnant women.

At the present time several methods are used to determine the phosphatase activity of the blood.^{15, 16, 21} These are essentially similar in principle. They consist in measuring the phosphorus set free as inorganic phosphate when the enzyme present in the blood is allowed to act on a phosphoric acid ester substrate under standard conditions. Unfortunately there is at present no general agreement in reporting results so that it is difficult to convert one group of findings into another. We have used in our work a slight modification of the method employed by Roberts.¹⁶ This method is as follows: The determinations are made on fasting blood. Two cubic centimeters of plasma (citrated blood) is mixed with 2.3 c.c. of distilled water and 0.7 c.c. of N/10 sodium hydroxide. This produces a pH of approximately 8.9. To this is added 1 c.c. of a 1 per cent solution of sodium beta-glycerophosphate. The mixture is then incubated at 37.5° C. for two hours, after which its inorganic phosphorus content is determined by the method of Fiske and

the sixth month, and here for the first time individual values above normal are obtained. In the eighth and ninth months the values become definitely elevated, averaging 8.33 and 10.35 units, respectively. Only exceptionally in these two months is a value obtained which lies within the range of normal for the nonparturient woman. † During labor the values average at even higher levels, 12.53 units. Postpartum the phosphatase values fall rather abruptly, reaching average levels of 6.9 units at the end of ten days. This latter value is still above normal, and the group contains a considerable number of cases with readings markedly above normal. The high levels found in the last months of pregnancy are in general agreement with the reported findings of Cayla and Fabre,²³ whose work came to our attention after our own investigations had been completed. These workers studied a small group of parturient and nonparturient women. They found that the average blood phosphatase for the nonparturient women by their technic was 16 units per liter of blood. In their group of parturient women of approximately the same age levels they obtained average blood phosphatase values of 36.4 units per liter of blood in the seventh month of gestation, and average combined values of 38.8 units per liter of blood for the eighth and ninth months.

A few studies of blood phosphatase in the newborn and in infancy are available. Stearns and Warweg²⁴ in a thorough study of the blood phosphorus, calcium and phosphatase from birth to maturity found that the plasma phosphatase at birth was low and rose abruptly to a maximum during the first month. Bodansky²⁵ in a later study on newborn puppies found high values, averaging about 40 units (normal 1.5 to 3 units for adult dogs) at birth and for about four hours thereafter.

∧ We have done 15 phosphatase determinations on cord blood (Table I). These values average 5.00 units, with a range of from 1.84 to 6.64 units, values that are lower than the normals for children. The average for children is about 7.5 units and ranges up to 15 units by our technic.

Blood phosphorus determinations were done on all cases. On the whole these values remained essentially constant throughout, though at a slightly low normal level. No significant difference was observed in the blood phosphorus values of the last two months of gestation. The relatively high phosphorus values in the cord blood and the generally elevated phosphorus values in the postpartum period are noteworthy.

∧ From the results listed in Table II it would appear that there is no significantly consistent difference between the phosphatase values in the blood of women bearing males and those bearing female children. Nor does the season of the year of birth appear to affect significantly the blood phosphatase or phosphorus values. Our work with the blood calcium has been too inadequate for analysis in regard to seasonal variations. ∨ Nor were the weights of the delivered fetuses or the degree of gravidity of the mother significantly correlated with the phosphatase values.

white women there is a seasonal variation in the calcium and phosphorus values, the values during the months of January to May averaging less at every stage than those during the remaining seven months. In Table II we have therefore listed the phosphatase values according to the sex of the newborn and to the season of the year of their birth.

DISCUSSION

A study of Table I discloses that the blood phosphatase values during the first six months of pregnancy lie within normal limits. The average values in the seventh month appear significantly different from those of

TABLE II. RELATION OF PLASMA PHOSPHATASE TO SEX OF CHILD AND SEASON OF YEAR OF BIRTH

SEASON OF YEAR OF BIRTH	MONTH OF GESTATION	AVERAGE PLASMA PHOSPHATASE UNITS/100 C.C. BLOOD PLASMA			AVERAGE PLASMA PHOSPHORUS MG./100 C.C. BLOOD PLASMA	
		MALE	FEMALE	BOTH	MALE	FEMALE
April to October	8th	7.92	7.65	7.84	3.25	3.02
	9th	9.27	11.06	10.16	3.14	3.00
	Before*	12.09	13.19	12.64	3.15	3.30
November to March	8th	8.73	8.33	8.50	3.14	3.12
	9th	11.17	9.89	10.53	3.07	3.08
	Before*	13.14	11.73	12.43	3.16	3.00

*Taken while patient was in labor.

TABLE III. PLASMA PHOSPHATASE OF UNUSUAL CASES

AGE OF MOTHER	NUMBER OF PREGNANCIES	MONTH OF GESTATION	UNITS OF PLASMA PHOSPHATASE/100 C.C. PLASMA	REMARKS CONCERNING PRESENT PREGNANCY
36	1	Before*	22.36	Triplets, 1 dead
35	3	Before*	8.08	Macerated dead fetus
44	1	8th	5.98	Premature, died
18	1	9th	11.60	Macerated dead fetus
34	2	9th	11.60	Living twins
25	3	9th	13.00	Living twins
27	3	9th	13.38	Living twins
19	1	9th	11.90	Living twins
27	2	9th	12.60	Living twins
24	2	9th	9.72	Living male, preeclamptic Toxemia
34	8	Before*	9.80	Living twins
32	3	9th	11.49	Preeclamptic toxemia
35	5	Before*	14.56	Living male
27	5	9th	8.07	Preeclamptic toxemia
37	3	Before*	9.72	Living female
29	3	9th	8.72	Preeclamptic toxemia
32	2	9th	11.13	Living male, hypertension
37	3	Before*	12.96	Living male, hypertension
24	4	Before*	12.52	Living female, hypertension
45	1	9th	14.74	Living female, hypertension

*Taken while patient was in labor.

will lay the groundwork for the development of rickets in the fetus and infant. At the present time we are engaged in a series of investigations designed to throw light on this question.

Finally, we cannot attribute the elevation of the blood phosphatase in the last two months of pregnancy to the coexistence of liver disease or jaundice in the mother. None of our patients were jaundiced, nor were they suffering from any of the other diseases known at the present time to be associated with an elevation of the blood phosphatase. It will also be seen from a study of Table III that in the few cases with hypertension, and preeclamptic toxemia, the blood phosphatase values did not vary significantly from the average.

SUMMARY

1. Blood phosphatase determinations were done on 201 cases of normal pregnancies representing all of the months of gestation.

2. The average blood phosphatase values were found to be definitely higher than normal in the last two months of pregnancy and during labor.

3. Relatively low phosphatase levels were found in a small number of determinations in cord blood.

4. There was no significant relationship observed between the blood phosphatase levels and the sex of the newborn or the season of the year of their birth.

5. The possibility that the blood phosphatase levels may reflect normal or early abnormal phases of bone metabolism in the mother or fetus is discussed.

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In Table III we have listed the findings in those cases of pregnancy which deviated from the usual in some respect. Though not necessarily significant, it is interesting that with one exception the maternal blood phosphatase values of the cases of twin pregnancies were above average and that of the instance of triplets decidedly above average. The other conditions listed did not appear to affect the phosphatase findings significantly.

The rise in the blood phosphatase in pregnancy, particularly in the last three months, may be variously interpreted. It is clearly established that the process of ossification in the developing fetus is at its height in these last three months. Givens and Macy²⁶ have shown by a series of laborious analyses that the greatest fetal demand for minerals occurs during the last three months of gestation. It can therefore be concluded that the last trimester is the period of greatest activity in fetal ossification and therefore presumably the period of greatest phosphatase need. That this fetal need exists is supported by the finding of high blood phosphatase values in infancy and childhood, the periods of great activity of bone formation.^{24, 25} However, the low values found by us in the cord blood, figures which represent composites of maternal and fetal values, may indicate that the fetus, in utero at least, is unable to provide sufficient amount of the enzyme phosphatase for its needs, and that the high values found in the maternal blood during the last months of gestation may represent a successful compensatory response in the mother.

Or are these elevated values to be regarded as delicate indices of potential or actual preclinical disorders in bone metabolism in either mother or fetus? Except in normal periods of increased ossification in infancy and childhood, blood phosphatase values above the accepted normal usually indicate abnormal or immature ossification, as in Paget's disease and rickets. That the last three months of pregnancy are crucial for the maintenance of the integrity of the bone metabolism of the mother is evident from the numerous clinical reports of dental caries, of reports of osteoporosis, and the occasional occurrence of maternal osteomalacia. This period is equally critical for the fetus. We have already called attention to the existence of cases of fetal rickets. Do therefore the elevated blood phosphatase values represent a pathologic or potentially pathologic state of bone metabolism in mother or fetus?

Since the phosphatase values of the cord bloods were low, the high maternal phosphatase values, prior to delivery, can be interpreted only as being predominantly of maternal origin. Stearns and Warweg²⁴ find low values in the newborn immediately after birth. Hence the fetus appears to be elaborating very little of the enzyme phosphatase, and, in utero, apparently is dependent upon its mother for its requirement of this enzyme. It is possible that the normal development of the fetus is dependent upon an adequate supply of the enzyme phosphatase by the mother and that an inadequate supply of this enzyme in utero

3. Preeclamptic toxemia at six and one-half months developed postpartum toxic psychosis with recovery.
4. Preeclamptic toxemia.

The first three each accounted for a fetal death. There was no maternal mortality.

TABLE I

INDICATIONS	CLASSICAL		CLASSICAL WITH HYSTERECTOMY	
	PRIM.	MULT.	PRIM.	MULT.
1. Contracted pelvis	121	8	-	-
2. Previous section	-	72	-	38
3. Disproportion	61	7	-	-
4. Elective	41	7	2	2
5. Toxemia	31	1	-	-
6. Previous difficult delivery	-	17	-	7
7. To sterilize	1	11	-	16
8. Placenta previa	4	4	-	1
9. Abruptio placentae	3	2	1	1
10. Fibroids	2	3	4	1
11. Pelvic injury	4	-	-	-
12. Cardiac disease	3	1	-	-
	271	133	7	66
	404—84%		73—15.3%	

In listing the definite reasons for cesarean, it must be borne in mind that in some 60 instances there were contributing factors which were of secondary importance, but nevertheless convinced the operators of the advisability of the elected procedure.

CONTRACTED PELVES (129 CASES)

An arbitrary standard of measurements was set in order to give a definition of contracted pelvis. Any patient whose measurements were below this standard was listed. Funnel pelvis accounted for 100 cases, flat pelvis for 21 cases, and just minor for 8.

In this group were 121 primiparas of whom 18 had had a test of labor. Of the 8 multiparas, 3 were allowed a test of labor. The classical operation was done in every instance. No maternal mortalities were resultant in this group but there occurred 4 fetal deaths due to: (1) Congenital heart, 2; (2) question of cerebral hemorrhage, death two days postpartum; (3) no cause known, baby died one month postpartum. One set of twins was delivered.

There were 4 patients who developed serious morbidity; 1 developed a thrombophlebitis; 2 had acute mastitis necessitating drainage in one; and one patient had an active pyelitis with metastatic abscesses in the neck. Induction of labor had failed.

In a series of 4,142 women who had vaginal deliveries by the same operators, there were 25 fetal deaths (19 per cent) following difficult forceps deliveries. These were patients who had no other contributing factors such as toxemia, etc., and who were at term. With this knowledge in mind, and in the interests of the child, the operators were more prone to section the woman with a contracted pelvis without any test of labor.

PREVIOUS SECTIONS (110 CASES)

This group consisted of 110 patients, 72 of whom had the classical operation and 22 of the 72 had tubal ligation. Two individuals were allowed a moderate test of

AN ANALYSIS OF 482 CESAREAN SECTIONS IN PRIVATE PRACTICE

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MUCH discussion has been elicited because of the increasing number of sections being done throughout the country. There is no doubt that the indications have been liberalized. Many of us have yielded to the pressure brought to bear by patients who have no intention of having more than two or possibly three children and who do not propose to lose the present incumbent, as it were, during the course of a difficult labor. To go into all the sociopsychologic bypaths which have led to this current frame of mind is not my intention.

We are confronted with the fact that many men are operating who are not qualified to judge when operation is indicated nor trained to operate. This partially accounts for the excessively high maternal mortality following cesarean section which is reported for this State and for the country as a whole. The present trend for operative deliveries is rapidly becoming the recognized procedure, as far as the laity is concerned, and the general practitioner is compelled to keep step. All of us hear patients say that they would much rather have a cesarean because it is so much easier, and they are sure to have a baby to show for their time, effort, and monetary output.

The present report is given in order to analyze cesarean section under more favorable conditions. First: it deals with a so-called higher class of patients well above clinic or even general practice average; second: practically all of the patients have had adequate prenatal care; third: the operating has been done by well-trained obstetricians with a uniformity of technic and training. Furthermore there are more cesarean sections followed by hysterectomy in this series than in any report I have seen to date.

This series of sections is taken from a group of 4,979 deliveries of patients six months pregnant or over, a cesarean incidence of 9.68 per cent as compared with the general hospital percentage of 2.9 per cent as given by Dr. Maxwell's report of three years ago. In this group are listed 404 classical sections, 73 with hysterectomy, 1 low cesarean, and 4 vaginal hysterotomies. The last five will be included in the general average but will not enter the general discussion. The low section was done for a relative disproportion, with no mortality. The 4 vaginal sections were done for the following reasons:

1. Premature rupture of membranes with uterine inertia at six months.
2. Premature separation of the placenta at six months.

Of this group 10 were multiparas. Two elderly primiparas had hysterectomy. Two fetal deaths occurred and one mother died of a postoperative ileus. Three patients developed secondary wound infections and one had a moderate postpartum hemorrhage.

TOXEMIA (34 CASES)

What to do about the toxic patient is always a debatable subject. Of 4,624 deliveries there were 168 cases of toxemia varying from a mild albuminuria or slight rise in blood pressure to the fulminating eclamptic patient. Approximately 1 out of 3 of these patients was sectioned. This group was divided into the eclamptic and the preeclamptic type patient, depending upon the presence or absence of convulsions or coma. There were 12 eclamptic patients, all primiparas, with 2 infant deaths at six and six and one-half months and no maternal deaths. The preeclamptic patients were 22 in number, with 20 primiparas, 2 of whom had vaginal hysterotomies. Three fetal deaths occurred: one premature at six and one-half months following vaginal hysterotomy and 2 at seven and one-half and eight months, respectively, following the classical operation. Two sets of twins were delivered. The recorded morbidity ran rather high in this group and was characterized by the large number who developed postoperative convulsions, 9. Other complications were: 1 infected wound, 1 postoperative ileus with recovery, and 1 temporary anuria.

The fact that 4 out of 5 of the fetal deaths were due to prematurity associated with toxemia would seem to substantiate the idea that a vaginal delivery of some type, even though destructive to the fetus, should be done on toxic patients who are not near term. The consideration of the baby is distinctly of secondary importance in this instance.

PREVIOUS DIFFICULT DELIVERY (23 CASES)

There were 23 patients who had one or more very difficult vaginal deliveries with the loss of the babies and some with severe lacerations. Sixteen classical operations and 7 sections with fundectomy were done, with one set of twins. In one instance both the mother and the baby died. Maternal death was due to cerebral thrombosis eighteen days postpartum. She was given a test of labor but there was failure of the presenting part to engage. Though the baby was at term it was stillborn. A number of rather serious sequelae followed operation in this series of cases: (1) Infected abdominal wound; (2) acute dilatation of the stomach; and (3) postpartum toxic psychosis with recovery.

PLACENTA PREVIA (9 CASES)

Of 20 cases of placenta previa encountered in 4,624 patients, 9 were sectioned. 8 by the classical method and 1 with hysterectomy. There were 4 primiparous and 5 multiparous women with no maternal deaths. Two babies died of prematurity at six and six and one-half months.

ABRUPTIO PLACENTAE (9 CASES)

Premature separation occurred 22 times all told. Cesarean operation seemed indicated and was done on 9 patients, 5 classical, 2 with amputation of the fundus, and 2 vaginal hysterotomies. Of these, 4 women were in their first pregnancy. No mother died but two babies did, both prematures operated by cesarean section with fundectomy and vaginal section. There was no untoward morbidity in either of the hemorrhage groups.

FIBROIDS (10 CASES)

Of the 10 women who had fibroids, 5 had a hysterectomy and the remainder, 2 primiparas and 3 multiparas, the classical operation with myomectomy. No mortalities were recorded though one patient acquired a postoperative phlebitis and one was in rather severe shock followed by good recovery.

labor but made no progress. One mother died of intestinal obstruction nine days postoperative. Her previous surgery consisted of a classical cesarean which was done for contracted pelvis.

No fetal deaths occurred. Two patients developed a moderate postoperative fever with good recovery; two had an acute mastitis without further complications; and one had perineal abscesses due to infected hemorrhoids. Thirty-eight sections with hysterectomy were done with no deaths and no serious morbidity. There was one set of twins.

It is interesting to note that of the 60 patients who had had previous sections and were sterilized either by tubal ligation or fundectomy, 51 elected to be sterilized following only one previous cesarean section. Granted that a certain number of the sections with hysterectomy were done because of adhesions, still the tendency was to limit the family to two children.

TO STERILIZE (28 CASES)

Of the patients sterilized, 12 had tubal ligation with no deaths and only one developed a moderate postoperative fever. The remaining 16 individuals had cesarean section and amputation of the fundus with no fetal, but one maternal death. No known cause could be found why she should die. Her first baby was lost following a difficult forceps delivery and she requested sterilization.

RELATIVE DISPROPORTION (69 CASES)

Of those individuals classified in this group, all had normal pelvic measurements but were sectioned for one of two reasons: first, failure of the presenting part to engage due to postmaturity, hydramnios, etc.; second: when, following engagement, there was no progress due to cervical dystocia, ineffective uterine contractions or other local causes.

Of the 69 patients sectioned for disproportion, 61 were primiparas, and 24 of these had a test of labor varying from six to thirty hours. Seven of the 8 multiparas were given a test of labor. No maternal deaths occurred but one baby died of congenital heart. All of the operations in this group were of the classical type. Morbidity was noted 3 times, twice when the abdominal wall became infected and partially separated; and once when the patient developed some elevation of temperature. An attempt to apply forceps had been made prior to operation in the last instance.

The great majority of individuals who had contracted pelvis or a relative disproportion and were given a test of labor, were watched very carefully in the hospital. Operation was advised before the mother became too exhausted or the chances for the baby were unduly diminished.

ELECTIVE (52 CASES)

Elective cesarean section was based upon the following causes:

Elderly primiparas	21
Personal request	12
Prolapsed cord	4
No cause given	4
Hematuria	2
Uterine inertia	2
Acute massive edema of external genitalia	2

One each of the remainder:

Elderly primipara, transverse position, dextrotorsion of the uterus
 Transverse position, cervical displacement from previous operation
 Tuberculous hip with ankylosis
 Prolonged sterility treatment
 History of endometriosis

2. Classical section because of a fulminating tuberculosis, patient died five days after operation.

3. Classical section because of endocarditis and to save labor; patient died eight hours postoperatively of cardiac failure.

4. Low cesarean section for relative disproportion; no cause known for death.

A review of the maternal deaths following vaginal deliveries (11 or 0.24 per cent) shows that the mortality represents a cross-section of maternal deaths due to be expected, i.e.: toxemia (2); cardiac disease (2); pelvic cellulitis (2); and one each of the remainder: hemorrhage from rupture of the uterine artery, acute pyelonephritis; fulminating pneumonia; pachymeningitis; and cause unknown. After a careful check on these cases there were none in which a cesarean section was indicated.

It will be noted that the deaths occurring in the controlled series of cesarean sections were not obstetric but surgical and that the death rate is about what one might expect following a series of abdominal operations which are not too radical. The referred patients more nearly represent the type of individuals and the problems encountered in clinical work.

FETAL DEATHS

In comparing the fetal deaths of the controlled group with those of the referred group we again find a difference in the cause of death.

In the group who were under constant supervision, there were 17 fetal deaths or 3.51 per cent. Ten were due to prematurity of which 8 were before the seventh month; 5 toxemia cases, 4 hemorrhage; 1 premature rupture of the membranes.

TABLE II. RELATION OF MATERNAL AND FETAL MORTALITY TO OPERATIVE INDICATION AND TYPE OF OPERATION

INDICATION	NUMBER CASES 482		MATERNAL MORTALITY 0.826%		FETAL MORTALITY 3.51%	
	CLASS.	CLASS. WITH HYSTEREC- TOMY	CLASS.	CLASS. WITH HYSTEREC- TOMY	CLASS.	CLASS. WITH HYSTEREC- TOMY
Contracted pelvis	129	0	0.0	0.0	3.10	0
Previous section	72	38	1.4	0.0	0.0	0
Disproportion	69	0	0.0	0.0	1.45	0
Elective	48	4	2.08	0.0	2.08	0
Toxemia	32	0	0.0	0.0	12.50	0
Previous difficult labor	17	7	6.25	0.0	6.25	0
To sterilize	12	16	0.0	6.25	0.0	0
Placenta previa	8	1	0.0	0.0	25.0	0
Abruptio placentae	5	2	0.0	0.0	0.0	50
Fibroids	5	5	0.0	0.0	0.0	0
Pelvic injury	4	0	0.0	0.0	0.0	0
Cardiac disease	4	0	0.0	0.0	0.0	0
Total	404	73	0.74%	1.36%	3.22%	1.36%

Three cases of congenital heart disease and 4 miscellaneous cases were reported: 1 of these died 1 month postpartum; 1 of enlarged thymus and atelectasis; 1 of possible cerebral hemorrhage; 1 stillborn following a test of labor with failure to engage.

MISCELLANEOUS (8 CASES)

There were 8 other patients, 7 primiparas and 1 multipara, who complete the list of cesarean sections. Four of these had had pelvic injuries which made normal delivery very questionable and 4 were severe cardiac patients, one of which was kept in bed for two months prior to delivery. All had the classical operation. One cardiac patient was sterilized by tubal ligation. No mortality or morbidity occurred.

TYPES OF OPERATION

The distribution of the types of operation is of interest. Of 404 classical sections 271 were primiparous and 133 were multiparous women. On the other hand only 7 of the 73 cesarean sections with hysterectomy were primiparas.

Incidental operations performed were as follows: tubal ligation 41 (5 primiparous and 36 multiparous women); appendectomy, 57; myomectomy, 13; hernia, 2; bilateral salpingo-oophorectomy, 1; left oophorectomy, 1.

MATERNAL DEATHS

In reviewing the maternal deaths in this series of 482 cesarean sections, there were 4 deaths or 0.826 per cent. Listing these cases:

1. Classical section on an elderly primipara with heavy muscles but normal measurements, death due to postoperative ileus (question of obstruction).

2. Classical section because of previous section which had been done for funnel pelvis, death due to intestinal obstruction.

3. Cesarean section with fundectomy in order to sterilize because patient had had two difficult deliveries before, though normal pelvis, and did not want any further pregnancies, no known cause was made out for her death.

4. Classical section on a patient who had previously lost two babies following difficult breech deliveries, death due to cerebral thrombosis, the first attack nine days postpartum and the second attack eighteen days postpartum.

Further analysis shows that among these deaths there were no cases in which any accessory operation had been done. Even where the accessory operation could be considered a contributing factor, I have been unable to find any increased morbidity. As a whole, it was noted that the patients who had cesarean section with hysterectomy tended to have a quieter and easier convalescence.

In those patients who were to be sterilized following previous section, cesarean section with amputation of the fundus was, in a number of instances, selected because of numerous adhesions. This no doubt prevented further adhesions and possible obstruction. Rupture of the uterine wall did not occur.

In this report all the referred cesarean sections were isolated in order that some comparison of the results might be made. They are not included in the previous figures. The 76 individuals of the referred group had been under the care of some outside physician, who in turn brought them for consultation. In this group are found 4 deaths (5.3 per cent mortality) and one patient who died of fulminating pneumonia. A postmortem cesarean section was done, in vain, to save the baby. Three of the other four were extremely sick before operation:

1. Vaginal hysterotomy, patient had been in a semiconscious state for one week before operation. Bag induction was attempted at six and one-half months without success. She died a few hours postoperative without gaining consciousness.

THE USE OF THE FEMALE BITTERLING AS A TEST FOR MALE HORMONE*

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CRITIQUE OF RECENT EXPERIMENTAL WORK

RECENTLY there have been many contributions to the literature concerning the lengthening of the ovipositor of the female bitterling. It is generally conceded today¹⁻⁵ that this remarkable phenomenon, in which the female of this species of fish extrudes a long ovipositor, can be used as a definite biologic test for hormones found in urine.

We have found, in contradistinction to Kanter, Bauer, and Klawans and others who claim that the fish is a test for estrogenic hormone, that it actually is a test for the male hormones.^{6, 7} Fleischmann and Kann, Ehrhardt and Kühn, Szusz, and other European investigators are responsible for the early work on the bitterling, while Kanter and others as well as ourselves were among the first in the United States to attempt to give the bitterling test medical significance. Kanter, Bauer, and Klawans in December, 1934, published a short article in the *Journal of the American Medical Association* entitled "A New Biologic Test for Hormones in Pregnancy Urine."⁸ This application of the fish test to pregnancy immediately attracted a throng of investigators including ourselves, who very quickly proved that the bitterling test was not a pregnancy test.⁹ Our stand has been corroborated by Gottlieb and others.^{10, 11} In their second and most recent article entitled "Hormonal Studies with the Ovipositor Lengthening Reaction of the Japanese Bitterling,"¹⁴ Kanter, Bauer, and Klawans suggest that we misinterpreted the statements in their first article. They insist that they had not intended to convey the impression that this is a test for pregnancy. However, the following quotation from their first paper will indicate that our interpretation had a real basis: "It was deemed advisable to run the fish test parallel to the Friedman test in order to determine the relative merits of the two" and "This test (female bitterling) will prove of clinical value over the Aschheim-Zondek and the Friedman test."¹² Whatever the explanation they attempt to offer as to the reason for comparing the fish test with the accepted pregnancy tests, it may be mentioned here that the basis of the established pregnancy tests (Aschheim-

*This work was carried out with the aid of a grant from the Lucius N. Littauer Foundation, Inc.

Of the 78 babies in the referred group, there were 11 deaths (14.05 per cent). Five of these were listed as premature and four as stillborn, two due to placenta previa, one due to prolapsed cord with asphyxia and 1 whose mother was eclamptic. The miscellaneous group consisted of 2 babies; one died following a postpartum cesarean section and one died several days postpartum, cause unknown. Two sets of twins were delivered.

The vaginal deliveries of 4,142 patients over six months pregnant with 4,176 babies gave a maternal mortality of 11 or 0.24 per cent and a fetal mortality of 132 or 3.18 per cent.

SUMMARY AND CONCLUSIONS

1. A series of 482 cesarean sections in private practice is reviewed, 404 classical, 73 with hysterectomy, 4 vaginal and 1 low, with a maternal mortality of 0.826 per cent and a fetal mortality of 3.51 per cent.

2. With proper supervision, adequate judgment and good surgical technic the maternal mortality can be kept at the minimum to be expected when the abdomen is opened.

3. It would seem that more effort should be made to deliver the premature toxic patient vaginally inasmuch as the chances for the fetus are greatly diminished. Possibly vaginal hysterotomy might be employed more frequently.

4. When sterilization is indicated and there are numerous pelvic adhesions, cesarean section with fundectomy is to be seriously considered, since it aids in convalescence and prevents the formation of more adhesions.

5. Fetal death rate after eliminating the unavoidable deaths such as prematurity, congenital heart, etc., should be very low. In this series it was 1.25 per cent.

I wish to thank Dr. F. M. Loomis and Dr. J. W. Sherrick for the majority of the source material on which this paper is based.

2923 WEBSTER STREET

Kishori Mohan Pal: Vesico-Vaginal Calculus in a Nullipara, Calcutta M. J. 30: 102, 1935.

A case of vesicovaginal calculus is reported in a fifteen-year-old, married, nulliparous Hindu girl, a vegetarian. No history of previous illnesses, and no family history of calculus. Chief complaints were vaginal discharge, incontinence of urine for one year, urinary frequency since five years, pain in lower abdomen and dyspareunia. Examination revealed a large calculus, partly visible at introitus, impacted in vagina, and continuous with a smaller portion in the bladder through a vesicovaginal fistula. Stone, removed by operation, weighed 5½ ounces and in its greatest portion was 7.5 cm. by 6.5 cm. This condition is a rarity. Only two cases of vesicovaginal calculus are reported in the literature: nine of vaginal type are described. The origin of the stone is questionable. Some believe it has a primary vesical formation, others a vaginal origin.

F. L. ADAMS AND S. A. PEARL

Their explanation of the bitterling test is evidently untenable. It is the one first put forth by Fleischmann and Kann and recently disproved by Ehrhardt and Kühn. The latter showed⁵ that Kanter, Bauer, and Klawans were mistaken in considering this test as a test for estrogenic hormone. They obtained unsatisfactory results with the bitterlings, using urines from pregnant mares which are known to contain tremendous amounts of estrogenic substances, and which is the commercial source of many of our common therapeutic hormone preparations.

The histologic and anatomical remarks of Kanter, Bauer, and Klawans also deserve some notice. They maintain, "The ovipositor has the histology of the human cervix uteri. Under stimulation there is a dilatation of the lumen, the blood vessels, and the lymphatic spaces, with occasional pigmentation but no actual cellular changes. The ovary and oviduct are unaffected by the artificial stimulants. If we may be allowed to draw analogies between the fish and the mammals, we see the same thing in the mouse, the rat, and the rabbit under estrogenic hormone stimulation, changes in the cervix and vagina with no noticeable effect upon the ovaries." However, Fleischmann and Kann¹⁵ studied the histology of the ovipositor some few years ago and found no resemblance to any pelvic organ of the mammal. They described the ovipositor as a thin tube the cellular structure of which resembles no part of the genital system in mammals. They maintained that it is regarded as a modification of the outer skin and is composed of an outer epidermis and cutis, and an inner thin lining of epithelial cells. It is generally accepted by ichthyologists* that the ovipositor is merely an external egg-laying tube of epidermal tissue and has no relation at all to the oviducts or the cervix uteri. Further, in the same paragraph Kanter, Bauer, and Klawans state that the ovaries and oviducts are not affected in the bitterling by the estrogenic substances, and yet it is well known that the oviducts are greatly affected in mammals upon being stimulated by estrogenic substances.

The results which Kanter, Bauer, and Klawans tabulate of various estrogenic hormone preparations and other glandular substances are interesting from several standpoints. We can corroborate many of their results which we had independently made. Thus, we obtained positive results in forty-eight hours with the bitterlings using doses of 45 and 135 R.U. of progynon tablets, 50 R.U. of aqueous commercial theelin and 200 R.U. of theelin in oil and irregular results with emmenin.† We also obtained negative results with antuitrin-S and A.P.L. Like Kanter, Bauer, and Klawans we obtained negative results in forty-eight hours with the pure crystalline female hormones, theelin and theelol. As is

*We are grateful to Mr. Christopher W. Coates of the New York Aquarium for this explanation and for his kind cooperation.

†We wish to acknowledge the generous supply of Progynon, Androsterone and Testosterone from Schering Corp., Bloomfield, N. J., and the Emmenin and A.P.L. from Ayerst, McKenna & Harrison, Rouses Point, N. Y.

Zondek and Friedman tests) is the presence of the hormones of the anterior lobe of the pituitary gland or the A.P.L. hormone in the urine of pregnancy in tremendous amounts. The fish have been shown not to react to stimulation by these hormones by many investigators, including Kanter, Bauer, and Klawans themselves. Kanter, Bauer, and Klawans now state: "As was feared it was immediately assumed by many of our readers that we were advocating a new biologic test for pregnancy and because of such misinterpretation the caution that was exercised in avoiding definite conclusions was apparently unavailing." They apparently do not heed their own warning, since in the third page thereafter we read: "In an attempt to evaluate the possibilities of the test upon the bitterling as a pregnancy test, we ran 132 consecutive specimens of urine parallel to the Friedman tests. . . . Table III shows the result of this study. The tests agree in 84.4 per cent of the cases." In their discussion at the end of the paper they state, "The test for estrogenic hormone using the ovipositor lengthening function of the Japanese bitterling* as the criterion has proved to be of value in detecting excesses of the hormone in the urine of females associated with pregnancy, endocrine disturbances, and chronic cystic mastitis." Again, "In attempting to use this reaction as a test for pregnancy, several precautions are advisedly given. . . . We feel that in conjunction with one of the other biologic tests the test upon the bitterling will prove of value as an aid in diagnosis where ectopic pregnancy, incomplete abortion, missed abortion, placental polyp, or any other condition where the death of the fetus is suspected." It is not to be wondered at that others misinterpret their remarks when they themselves do so. However, they show that 23 normal nonpregnant women out of 40 gave positive bitterling tests. We may thus use Kanter, Bauer, and Klawans' own records to substantiate our first contention that the female bitterling test is *not a test for pregnancy* no matter how well their pregnancy findings agree with the Friedman test.

Kanter, Bauer, and Klawans furthermore claim that "estrogenic substance is fairly firmly established as the exciting factor in the production of the phenomenon that constitutes the criterion for the test." They apparently do not realize that many things are estrogenic in nature, such as many vegetables, coal tar products, and many substances of varied chemical composition which are not hormones.^{12, 13} The male hormone derived from the testes, testosterone, which has no relation to a pregnancy test, is an estrogenic substance.¹⁴ Moreover, crystalline androsterone, which is the male hormone found in urine, has given markedly positive fish tests within twenty-four hours, and is not estrogenic in nature.¹⁴

*Here we reiterate that the Japanese and the European bitterlings are considered to be identical in ovipositor and ovulatory mechanism by the authorities of the New York Aquarium. We suggest the simple term "Female Bitterling Test" so as not to confuse this test with a male bitterling ecdysis test.

esis, neither we nor Kanter, Bauer, and Klawans have observed any spontaneous lengthening of a single ovipositor during the breeding season when the females were kept segregated from the males.

Realizing the unreliability of the fish test as a test for pregnancy, we have performed quantitative male hormone determinations on some thirty medical students who are normal male adults. We used twenty-four-hour urines only and were careful in the collection and the manner of obtaining the total daily outputs, so that we were able to determine with some degree of accuracy the amounts of male hormone excreted daily by normal males. The average amount of male hormone excreted was 30 to 40 bitterling units per day, while the normal variations were from 15 to 95 B.U. excreted per day.

The use of casual specimens as in the technic of Kanter, Bauer, and Klawans is not reliable from a quantitative standpoint. We have noted a positive and a negative result in two successive samples of urine from

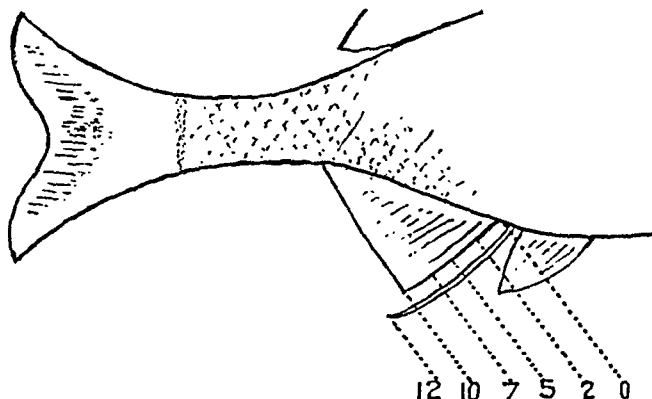


Fig. 1.—Scale used in measuring the length of the ovipositor of the female bitterling.

We tentatively define a bitterling unit as the amount of material which when added to a tank containing two female bitterlings in 4 liters of water, produces an increase in growth of 7 or more on our scale in one of the two fish. The scale used is as follows: an ovipositor which is not visible is 0; if equal in length to that of the anal fin the reading is 10; if half the anal fin, 5, etc. (i.e., ten times the ratio of the length of the ovipositor to that of the anal fin) (Fig. 1).

the same patient taken at hourly intervals. It must also be observed that many urines are toxic to the fish. However, the simple expedient of dialysis of the urine against running water renders all urines non-toxic.¹⁷

Further quantitative work will be done as soon as the fish's spawning season is over, since we have noticed each year conflicting results occurring during tests made in the breeding season. Pathologic cases will be of especial interest with particular reference to therapy in dysfunctions of the endocrine system.

SUMMARY

It is shown that the lengthening of the ovipositor of the female bitterling by external stimuli cannot be considered to be a test for estrogenic hormones per se. There are substances excreted in most normal urines

well known, these are estrogenic and in explanation of their inactivity they suggest that "in the crystallization process, changes take place in the estrogenic products that decrease the efficiency of their action upon the ovipositor of the bitterling." It is surprising that over 2,000 R.U. of estrin require two weeks to produce a positive fish test while relatively few capon units of the *crystalline* male hormones, androsterone or testosterone, give a positive fish test in forty-eight hours. Furthermore, the reliability of any reaction which is noted after ninety-six hours is very doubtful, inasmuch as regression of even exceptionally long ovipositors usually begins before that time. We must therefore disregard all of Kanter, Bauer, and Klawans' positive reactions which are recorded after ninety-six hours.

Kanter, Bauer, and Klawans also mention a personal communication from Norris J. Heckel who "has found that normal adult male urine gives positive tests using the technic that we have described but if the amount of urine is decreased the tests become negative." This corroborates our findings with male urine as reviewed below.

EVIDENCE FOR THE USE OF THE FEMALE BITTERLING AS A TEST FOR MALE HORMONE

In April, 1935, it was shown that the work of Kanter, Bauer, and Klawans was not correct so far as the diagnosis of pregnancy was concerned.⁹ We then continued the investigation to find out exactly what was the responsible factor in this fish test. On Jan. 29, 1936,⁶ we showed that the fraction of extracted male urine which produced the fish test also produced the capon test, and the fraction which contained the female hormone produced no ovipositor change and no capon change. Both crude female and male fractions of normal male urine were estrogenic in nature.

Similarly, the urines of pregnancy were extracted for the male and female hormones and the male fraction was the only one to give the fish test. We are of the opinion that positive reactions caused by all the commercial products are due to male hormone contaminations. We have also tested other substances which are closely related to the male hormones and containing the cholane nucleus, namely, theelin, theelol, ergosterol, cholesterol, and sodium taurocholate,¹⁰ on the fish and no positive reactions were obtained. Slight effects were sometimes obtained with tremendous doses. To confirm the experiments with male hormone, synthetic crystalline androsterone and testosterone in very small amounts (0.6 to 1.2 mg.) gave positive results on the fish in forty-eight to seventy-two hours.⁷ To explain why male hormone is the causative factor is not a very simple thing; however, we believe that the male in its spawning season excretes its hormone in the vicinity of the female, and she is thereby stimulated to lengthen the ovipositor and thus deposit her eggs in a mussel. In support of this idea, which we realize is only an hypoth-

PROCEDURE

Five groups of normal obstetric cases were chosen. In order to determine the normal total period of bleeding during the puerperium, observations on a group of 50 cases were made daily and the length of time that bloody lochia persisted was recorded. This group was used as a control. A second group, consisting of 51 cases was then given snake venom injections and the same observations as to the persistence of puerperal bleeding made. The criterion used for the determination of cessation of bleeding was complete absence of discoloration of the lochia.

A third group of cases, 20 in number, were studied for normal blood loss at parturition, and here only cases of spontaneous, normal delivery without anesthesia or analgesia were observed. This group also served as a control, for comparison with a fourth group of 9 patients who were given snake venom constantly for from two to four weeks prepartum, and postpartum as well. The blood lost during delivery was carefully measured in both groups and the simplest method of collection was employed. This consisted in catching every drop of blood in varying-sized basins, and saving all sponges, pads, drapes, etc., used, from which the blood was subsequently squeezed out. The totals thus obtained were measured and recorded. This method was uniformly employed in all cases included in these two groups.

The injections of the venom were administered subcutaneously three times weekly to once daily and the dosage varied from 0.2 to 2 c.c., of a 1:3,000 solution in saline. In the early cases the initial dosage was 0.2 c.c., but due to the tendency toward localized skin reactions at the site of injections with this dose, the initial quantity given was changed to 0.5 c.c. Reactions in this way were almost completely eliminated. Injections of venom were given either until bleeding had completely disappeared, as in the postpartum cases, or until parturition occurred, as in the prepartum cases.

In order further to check the results obtained, a fifth group consisting of 13 patients were given ergoklonin by mouth, one teaspoonful 3 times daily for ten days following delivery. The effects of the ergoklonin as compared to the snake venom could then be evaluated.

In addition to the above studies, cord bloods from the newborn of those patients injected prepartum were collected at the time of delivery and turned over to Dr. Peck* for determination of the presence or absence of antivenins. This was for the purpose of showing whether or not the venom injected into the mother actually entered the fetal circulation.

RESULTS

The results can readily be seen by reference to the charts. The duration of puerperal bleeding in normal cases (Table I) was found to be much longer than is commonly believed, the actual period varying from nineteen to forty-nine days. Comparison of these cases with those which received venom during the puerperium shows the marked difference in the injected group. Here the duration of bleeding varied between seven and nineteen days. The fact that such large series of cases were observed with such uniform results should be sufficient for critical analysis.

The normal blood loss at delivery (Table II) varied from 155 c.c. to 340 c.c. Although the method used in these determinations was rela-

*The authors wish to express their appreciation to Dr. Peck for the supply of the snake venom used in this work as well as many helpful suggestions. The venom is now available commercially and is manufactured by Lederle & Co.

which initiate this phenomenon. We have shown that these causative agents are the male hormones and have established in a preliminary way the daily amounts excreted by normal male adults.

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EFFECT OF MOCCASIN SNAKE VENOM (ANCISTRODON PISCIVORUS) ON PARTURIENT AND PUERPERAL BLEEDING

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FOLLOWING the observation by Peek and Sobotka¹ that animals could be made refractory to the Schwartzman phenomenon² by injection of moccasin snake venom, Peek deduced that this effect was due either to some change in the blood vessel walls or to some effect upon the clotting factors of the blood. Upon this basis in 1932, he³ treated various hemorrhagic conditions in human beings with snake venom and obtained marked improvement in the conditions. Since that time Peek and Goldberger⁴ have shown the value of the treatment in functional uterine bleeding, Greenwald⁵ in thrombocytopenic purpura, and Dack⁶ and Goldman⁷ in excessive nasal hemorrhages. In their last two reports Peek and his coworkers^{8, 9} have correlated the results obtained in different types of bleeding, leaving little doubt as to the efficacy of this method of therapy.

On the strength of the work already done the use of snake venom suggested itself in obstetric bleedings, and accordingly investigations were undertaken to determine the effects produced by the material on the blood lost at parturition and during the puerperium.

TABLE III
CASES TREATED WITH VENOM BOTH ANTE- AND POSTPARTUM

PA- TIENT	AGE	PAR- ITY	DOSAGE OF VENOM INJECTIONS GIVEN ANTEPARTUM										BLOOD LOSS AT DELIVERY	DOSAGE OF VENOM INJECTIONS GIVEN POSTPARTUM				PERIOD OF POST- PARTUM BLEEDING		
			0.5	0.8	1.0	1.5	2.0	2.0	2.0	2.0	2.0	2.0		2.0	2.0	2.0	2.0		2.0	2.0
E. P.	27	3	0.5	0.8	1.0	1.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	6 days
A. F.	23	2	0.5	0.8	1.0	1.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	6 days
T. T.	26	2	0.5	0.8	1.0	1.5	1.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	6 days
B. K.	26	2	0.5	0.8	1.0	1.5	2.0	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	8 days
C. F.	27	1	0.5	0.8	1.0	1.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	5 days
R. P.	18	3	0.5	0.8	1.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	7 days
E. P.*	19	1	0.5	0.8	1.0	1.5	1.5	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	8 days
M. H.	33	1	0.5	0.8	1.0	1.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	7 days
J. C.	21	2	0.5	0.8	1.0	1.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	6 days

*Midforceps, difficult delivery followed by uterine atony.

tively crude, this factor is of no great importance in judging results since it was employed on all observations. The differences between the blood loss during parturition of noninjected cases as compared to those injected, is strikingly brought out by reference to Table III. In 7 of the 9 cases the blood loss was only from 15 to 100 c.c., 1 case lost 255 c.c., and 1, 500 c.c. In the latter, difficult midforceps delivery was followed by uterine atony. It is interesting to note that puerperal bleeding following puerperal administration of venom in large doses, 2 c.c. daily, was reduced to from five to eight days. Undoubtedly this dosage played an important rôle.

TABLE I
COMPARISON BETWEEN INJECTED AND CONTROL GROUPS OF CASES

	NO. OF CASES	NO. OF VENOM INJECTIONS	DURATION OF PUERPERAL BLEEDING (DAYS)
Controls	50	None	19 to 49
Injected cases	51	5 to 12	7 to 19

TABLE II
NORMAL BLOOD LOSS AT DELIVERY—CONTROLS. ALL CASES DELIVERED SPONTANEOUSLY WITHOUT ANESTHESIA

PATIENT	AGE	PARITY	LENGTH OF LABOR	BLOOD LOSS
1. J. D.	43	3	6 hr.	340 c.c.
2. C. C.	23	2	15 hr.	220 c.c.
3. I. M.	24	2	8 hr.	200 c.c.
4. G. M.	19	1	18 hr.	270 c.c.
5. A. D.	22	1	17 hr.	200 c.c.
6. A. O.	28	3	11 hr.	250 c.c.
7. V. E.	26	2	11 hr.	300 c.c.
8. E. W.	30	3	8 hr.	180 c.c.
9. L. R.	20	3	3 hr.	190 c.c.
10. C. M.	29	3	8 hr.	180 c.c.
11. M. B.	30	2	12 hr.	265 c.c.
12. E. Z.	23	2	10 hr.	165 c.c.
13. M. H.	26	3	5 hr.	205 c.c.
14. K. P.	30	4	7 hr.	155 c.c.
15. E. W.	27	1	9 hr.	295 c.c.
16. H. B.	22	2	19 hr.	265 c.c.
17. H. B.	33	3	16 hr.	210 c.c.
18. J. C.	33	1	5 hr.	220 c.c.
19. S. M.	27	1	4 hr.	180 c.c.
20. G. P.	23	1	15 hr.	215 c.c.

* Table IV shows the effect of ergoklonin administered to a group of 13 cases. All but one were bleeding at the time of discharge from the hospital on the tenth day postpartum.

The examination of the cord blood by Dr. Peek of patients injected before delivery failed to show the presence of antivenins, leading to the conclusion that the venom did not enter the fetal circulation.

It is to be stressed that at no time were any serious untoward effects observed which could be attributed to the administration of the snake

fore treated by venom may also be treated in the presence of pregnancy.

As is evident, further investigations are necessary before far-reaching conclusions can be drawn. The most important, it appears to the authors, is the determination of the mechanism by which the snake venom effects are produced.

SUMMARY AND CONCLUSIONS

1. The period of puerperal bleeding in a group of 51 cases receiving snake venom injections postpartum was materially shortened as compared to the duration of bleeding in a group of 50 controls.

2. The blood loss during parturition in a group of 9 cases which received antepartum injections of venom was distinctly decreased in comparison to a group of 20 controls. Postpartum administration of the material also lessened the period of puerperal bleeding in these cases.

3. Puerperal bleeding was present in all but one of the 13 patients treated puerperally with ergoklonin for at least ten days after delivery.

4. The inability to demonstrate the presence of antivenins in cord bloods obtained at delivery after prepartum injections of venom indicates that the material does not enter the fetal circulation.

5. No deleterious effects that could be attributed to the snake venom upon either mother or child were observed.

6. The use of this material is recommended in the severe anemias as well as other bleeding conditions associated with pregnancy, and especially where a previous history of excessive hemorrhages in previous pregnancies is obtained.

7. Although the results obtained up to the present are very encouraging, considerable work remains to be done before the material can be recommended for every obstetrical case. In the authors' opinion, the most important problem is the determination of the *modus operandi* of snake venom effects in the human being.

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venom. Localized skin reactions at the site of injections consisting of erythema and edema were occasionally noted in the early cases where small initial doses (0.2 c.c.) were employed, but these reactions quickly disappeared under simple treatment, and did not recur with subsequent injections. Peck and Rosenthal⁸ mention the not infrequent need for desensitization of patients, but in the series here presented this procedure was never necessary.

TABLE IV
EFFECT OF ERGOKLONIN UPON POSTPARTUM BLEEDING

PATIENT	AGE	PARITY	ERGOKLONIN ADMINISTRATION	LOCHIA DURING FIRST TEN DAYS POST-PARTUM
M. M.	23	2	Drams 1 three times daily	Bloody
R. K.	19	2	Drams 1 three times daily	Bloody
E. D.	30	2	Drams 1 three times daily	Bloody
A. S.	24	2	Drams 1 three times daily	Bloody
F. S.	25	1	Drams 1 three times daily	Bloody
H. O.	28	1	Drams 1 three times daily	Clear on ninth day
J. K.	27	2	Drams 1 three times daily	Bloody
A. W.	24	1	Drams 1 three times daily	Bloody
H. M.	28	4	Drams 1 three times daily	Bloody
C. M.	21	3	Drams 1 three times daily	Bloody
A. J.	26	3	Drams 1 three times daily	Bloody
J. G.	27	1	Drams 1 three times daily	Bloody
J. S.	35	3	Drams 1 three times daily	Bloody

COMMENT

Careful study of the tables presented shows such striking results that little comment is necessary. This is especially true of the controls and cases injected shown in Table I. Here the large series of cases leave little room for skepticism, and emphasize the efficacy of snake venom administration. Table III is extremely interesting because larger doses (2 c.c.) were used over long periods of time and the effects of both pre- and postpartum venom injections could be observed. Table IV, showing the results of ergoklonin given for 10 days after delivery, only serves to emphasize the effects produced by the venom.

From a practical point of view considerable work remains to be done before recommendations that snake venom be universally employed for the control of bleeding in obstetrics can be made. Since the exact modus operandi of this material is still unknown, the more familiar pituitrin and ergot must still represent the drugs of choice in the normal case. However, in cases of severe anemia where it is advisable to cut the blood loss at parturition and in the puerperium to a minimum, snake venom may prove extremely valuable, especially where there is a history of excessive bleeding during previous deliveries. It should also be given a trial purely empirically in postpartum hemorrhages, even though its effect may be delayed.

The fact that it does not produce deleterious effects in either mother or child is of great importance, since the hemorrhagic conditions hereto-

erythematous swelling at the injection site which appeared after eight to twelve hours. No general reaction was ever observed. Desensitization could easily be brought about by reducing the subsequent injections to 0.05 to 0.1 c.c. of the 1:3,000 dilution and gradually increasing to the 1 c.c. dose. In marked cases of hypersensitivity, the following series of injections may be given: 0.1 c.c. of 1:10,000; 0.4 c.c. of 1:10,000; 0.2 c.c. of 1:6,000; 0.4 c.c. of 1:6,000; 0.1 c.c. of 1:3,000; and 0.4 c.c. of 1:3,000. In the majority of cases the first suggested method was followed as it saved considerable time and was well tolerated.

It is important that therapeutically active venom be used. Previous reports have shown that the venom of individual moccasin snakes varies markedly in its content of the factor or factors responsible for the therapeutic effect.² At present, pooled venoms which are titrated on patients are used. It is necessary to bear in mind that venom solutions more than a year old should not be used.

MECHANISM OF ACTION OF VENOM

Previous clinical and laboratory experiments have clearly shown that circulating substances were not the cause of the antihemorrhagic effect produced by moccasin venom injections.³ The reversal of the positive venom test in purpura after treatment and the reduction in the size of the vessels in cases of hereditary familial telangiectasis as well as histologic studies seem to show that the venom has a direct effect on small blood vessels, making them more resistant to bleeding.^{4, 5}

Twenty cases of functional uterine bleeding treated with injections of moccasin snake venom are reported. Similar treatment was administered to five cases of uterine bleeding due to fibromyomas.

SUMMARY

Satisfactory clinical results were obtained in seventeen of the twenty functional uterine bleeding cases treated with the moccasin snake venom. The period of observation of these cases varied from two months to four years. Poor results were obtained in three cases. These are reviewed:

CASE 1.—Continuous bleeding was controlled. There was a decrease in the amount of hemorrhage and an increase in the free interval. However, this case was considered to be a poor result because the patient continued to have periods at two- to three-week intervals. The dosage in this case was inadequate.

CASE 2.—The period of treatment and observation was too short to warrant conclusions. This patient failed to return for further treatment.

CASE 3.—The treatment of this patient extended over a period of four years. A summary of her history is as follows:

A twenty-year-old girl whose menstruation began at eleven years of age. It occurred regularly every month for one week up to the age of thirteen, when severe

ADDITIONAL DATA ON THE TREATMENT OF UTERINE BLEEDING WITH SNAKE VENOM*

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IN A previous report the therapeutic effects of moccasin venom (*Anistrodon piscivorus*) in twelve cases of functional uterine bleeding were presented.¹ The clinical results obtained warranted further trial in cases of this kind. The present report embodies subsequent observations on some of the cases already reported, with the addition of new cases.

METHOD OF ADMINISTRATION

The moccasin venom was used in a 1:3,000 dilution with sterile sodium chloride (normal) containing 1:10,000 merthiolate. The venom was obtained through the courtesy of Dr. Raymond L. Ditmars of the New York Zoological Gardens.† The dosage and the method of administration have been modified.

All injections were given subcutaneously. The initial injection was 0.5 c.c. and subsequent injections were rapidly increased to 1 c.c. (by the third injection). The interval between administrations of the venom depended on the severity of the bleeding. It was advisable to give as much venom as possible the first ten days, because at about that time the majority of patients developed a sensitivity to the venom which necessitated a decrease in the amount until desensitization was accomplished.

There was a distinct quantitative relationship between the desired clinical effect and the amount of venom given. In cases with marked bleeding, 1 c.c. of the 1:3,000 dilution was given daily or even twice a day until the hemorrhage was controlled. In a number of the patients, daily injections were given at the beginning of the treatment. After the bleeding had been controlled the interval between injections of venom was increased so that only two or three treatments were given weekly.

If the subsequent menstrual period approximated the normal, two injections a week were administered for at least three normal menstrual periods. During the course of the treatment a maintenance dose had to be established.

In a number of the treated individuals a period of from six months to one year of normal menstruation occurred after the venom therapy had been discontinued. When metrorrhagia or menorrhagia recurred and venom was again administered, the initial dose was 1 c.c. If such a patient reported for treatment early enough, several 1 c.c. injections given two or three times weekly were found to be sufficient to bring about normal menstrual bleeding. It has also been noted that the course of injections necessary to control recurrences of bleeding was shorter than that necessary at the beginning of the treatment.

HYPERSENSITIVITY REACTIONS

In some cases a hypersensitivity to the snake venom protein occurred about the tenth day. This was characterized by an egg-shaped

*For lack of space detailed tabulations are omitted but may be found in the authors' reprints.

†Venom for clinical use can be obtained from the Lederle Laboratories.

This patient presented a complicated problem. She was a congenital cardiac, undernourished, anemic, and in extreme poverty. She had been treated by castration doses of x-rays to the ovaries and x-ray therapy to the pituitary and spleen and continued to have severe uterine bleeding. The venom treatment was used in the last four years. The result with this treatment during the last year and a half has been poor, yet we feel that without treatment she would have had increased uterine bleeding. This case demonstrated the effect of venom therapy administered over a prolonged period. Although the patient received relatively large doses of venom no toxic effects were manifest.*

UTERINE BLEEDING DUE TO FIBROIDS

Snake venom was also used experimentally in five cases of uterine bleeding due to fibroids. It was felt that in these cases venom had very little effect, especially if the fibroids were submucous. In several instances, although the bleeding was controlled at first, the venom became ineffectual with the increase in size of the fibroids.

CONCLUSIONS

1. Moccasin snake venom injections have been used with good results in seventeen of twenty cases of functional uterine bleeding.

2. The control of bleeding probably results by means of the action of the venom on the uterine capillaries, making these vessels more resistant to hemorrhage.

3. The method of treatment is offered as a procedure which will control functional uterine bleeding until there is a return to normal menstruation.

4. Adequate dosage based on clinical symptoms must be determined for each patient.

5. Moccasin snake venom has very little effect on uterine bleeding due to fibromyomas.

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*A polyp, 1½ by ½ inch, protruding from the cervix, was removed on September 2, 1936.

and alarming menometrorrhagia began. In the past seven years she has had six hospital admissions. Her treatments included (1) dilatation and curettage (hyperplastic endometrium and cystic degeneration were found); (2) parathormone, pituitrin, thyroid, insulin injections; (3) x-rays to spleen and pituitary; (4) in 1928 castration dose of x-rays to ovaries with moderate relief and then an exacerbation of the bleeding; (5) she was admitted to the hospital in July, 1934, with a hemoglobin of 35 per cent, and a transfusion was given.

Physical Examination.—Pallor; pulse, 92; blood pressure, 120/64; blood chemistry, basal metabolic rate and sugar tolerance test are all normal; Wassermann test, negative; thyroid, isthmus palpable; marked precordial thrill (felt in the fourth inter-space to left of sternum); heart enlarged to left; harsh systolic murmur over precordium; spleen not palpable; gynecologic examination, negative.

Course Under Venom Therapy (Chart 1).—A graph of the menstrual bleeding during venom treatment shows that from January, 1932 to June, 1932 she had regular, normal periods. This regularity continued up to May, 1933, although

GRAPH of UTERINE BLEEDING BEFORE and DURING TREATMENT
CASE 8

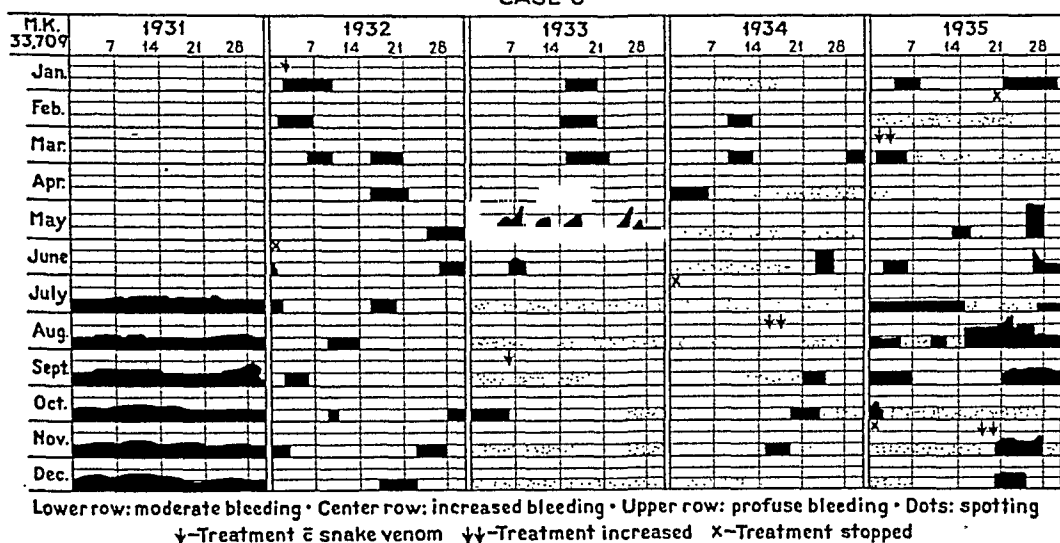


Chart 1.—A typical case of functional uterine bleeding treated with moccasin venom.

treatment had been stopped. In May, 1933, she had moderate to profuse bleeding for an entire month. In June she had a short period and then had continuous spotting in July and August, 1933. In September, treatment was resumed. The dose of venom was 1 c.c. three times a week, but this dose was insufficient as she continued to spot with varying free intervals. The dose was increased and in October, November, December, 1933 and January, 1934, the menstrual periods were normal. In April, May, and June, 1934 there was irregular spotting with a three-day moderate period in June. Treatment was not given in July as patient was on her vacation. In the middle of August, 1934, treatment was resumed and there were regular periods in September, October, and November. In December she spotted thirteen days. In January, 1935, she had two periods. In February there was irregular spotting and the patient was hospitalized for cardiac insufficiency. On discharge from the hospital, venom therapy was again administered and seemed to control her bleeding until the latter part of June when her periods became more irregular and profuse. The dose was then increased to 2 c.c. of the 1:3,000 dilution given four times a week and then further increased to 1 c.c. of 1:1,000 three times a week before bleeding was controlled.

In this five-year period there were 166,166 births reported to the Bureau of Vital Statistics. If to them be added 25 per cent to account for abortions, or 41,541, the total pregnancies in Philadelphia in the five years studied would have been 207,707.

Inquiry from the city's hospitals disclosed the fact that during the same interval fifteen cases of known chorionepithelioma had been admitted. The diagnosis in these cases had been made either from the extirpated uterus or curettings plus biologic tests.

The ratio of chorionepithelioma to pregnancy in Philadelphia during a five-year period was as one to 13,847 pregnancies or, roughly, 1 to 13,850.

Analyzing the fate of the 15 women, 8 died either immediately following operation or within a few months, of metastasis. Two were lost to sight and 5 remain well.

The immediate mortality, then, in the patients whose fate is known, was 53 plus per cent, while the salvage was a little better than 33 plus per cent, the result in the remaining two women being unknown.

In 8 of the 15 patients, the chorionepithelioma was preceded by a mole pregnancy, various times having elapsed between the mole and the chorionepithelioma, in one instance, five years. During the same five-year period 78 hydatidiform moles were found in the records of Philadelphia hospitals. Most patients were treated by hysterectomy, either supravaginal or total, with radium and x-ray postoperative.

The diagnosis was made from curettings in 9 of the 15 cases, and in 10 the Friedman test confirmed the findings. In the earlier cases this test was not routinely performed, but if one ignores these five, it will be seen that biologic estimation of the urine hormones was confirmatory in all but one, a case which presents so many points of interest in the diagnosis and management of this bizarre condition that it is reported in some detail.

CASE REPORT

L. G., thirty-three years of age, entered Kensington Hospital for Women, Feb. 28, 1933, complaining of vaginal bleeding, backache, bearing-down sensations. She had been in previous good health; had had two full-term pregnancies and one miscarriage five years before. (The patient failed to inform us, and it was not until after her death that it was learned, that the miscarriage described was really an hydatid mole.) The present illness began two weeks before admission, with an exacerbation of an old backache and irregular vaginal bleeding. There was some suspicion of a very early miscarriage. On examination the general physical condition was good. There was no abnormality in the blood or urine. The cervix was soft, the uterus large and boggy and retroverted to the third degree. A diagnosis of incomplete abortion with retroversion was made, and the patient was operated upon under avertin anesthesia.

The uterus was found subinvolved, retroverted. The appendix presented some evidence of catarrhal inflammation, and curettage revealed a moderate amount of spongy tissue. After appendectomy and Baldy suspension of the uterus, the patient made an uninterrupted recovery.

CHORIONEPITHELIOMA WITH ESPECIAL REFERENCE TO ITS RELATIVE FREQUENCY

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CHORIONEPITHELIOMA may well be termed a tumor of vagaries, both because of its often unpredictable degree of malignancy and because of the great variation in its incidence.

A third peculiarity of this neoplasm is the practical difficulty of reaching an accurate diagnosis from curettings, a number of tragic errors having resulted from this fact.

Since the development of the biologic tests for pregnancy, chorionepithelioma may generally be diagnosed by the persistence of a positive urinary reaction after abortion, labor or mole pregnancy, and especially if the test be positive with greatly diluted urine. However, even this diagnostic factor may fail, as will be shown in the history of the case here reported.

The incidence of chorionepithelioma is uncertain, many widely differing estimates having been made. In eighteen months' time, 7 cases were found among 2,700 autopsies in Vienna, while in Budapest not one case was found during a search extending over several years. Symmers states that in 12,000 autopsies performed at Bellevue Hospital, he did not encounter a single specimen of chorionepithelioma, and that in the fourteen years following the establishment of the pathologic laboratories in Bellevue, only one such tumor was discovered, this being a metastatic growth in the vagina.

To determine the incidence in one large city, we followed the plan of circularizing all the hospitals within the corporate limits of Philadelphia. It was thought that every case of chorionepithelioma developing in the city would sooner or later come to hospitalization, so that a fairly accurate census of all cases might be obtained. If these cases were checked against the total number of births reported to the Bureau of Vital Statistics during the same interval, the ratio of chorionepithelioma to pregnancy could be fairly well established.

This calculation made no provision for unreported abortions, and since it is commonly believed that one abortion to four full-term pregnancies is a reasonably correct proportion, 25 per cent of the number of births were added to them to obtain the total number of pregnancies.

The years 1929 to 1933 inclusive were studied, and so far as possible the subsequent life histories of the patients suffering from chorionepithelioma were followed.

it is important to note that operative procedures were inexcusably delayed by reason of the persistent negative biologic tests.



Fig. 2.—Section from the uterine wall at hysterectomy showing typical chorlonepithelioma.



Fig. 3.—The excised uterus filled with neurotic tumor masses.

The careful study of the foregoing case taken in connection with the others in this series demonstrates very clearly that positive Aschheim-Zondek or Friedman tests, especially with high dilution of urine in the

Microscopic examination of the curettings showed greatly degenerated placental villi which in places contained nests of syncytial cells varying considerably in size and shape (Fig. 1).

This tissue was regarded as somewhat suspicious and, accordingly, a Friedman test was made which was negative. The tissue was then submitted to a tumor conference and a diagnosis of deciduitis was returned.

Two months later the patient reentered the hospital stating that she had been having some slight vaginal bleeding daily since the operation. The pelvic examination was negative and upon curettage a few fragments of tissue were obtained. The laboratory report at this time states that the findings were similar to those of the previous curettings and that no evidence of chorionepithelioma was present. Another Friedman test at this time was negative.

On October 4 the patient reentered the hospital with a history that she had gone to the office of a neighborhood physician for a local treatment and had there



Fig. 1.—Curettings from which a diagnosis of deciduitis was returned. Friedman test was negative.

had a massive hemorrhage. On examination the uterus was found to be markedly enlarged, soft, with a mass of necrotic tissue projecting from the cervix. An attempt at digital removal of this mass resulted in furious hemorrhage, which necessitated an immediate transfusion and abandonment of any attempt at more radical operation.

The tissue obtained presented a typical picture of chorionepithelioma as illustrated in Fig. 2, and at this time the Friedman test was for the first time strongly positive. After two days a rapid vaginal hysterectomy was performed (Fig. 3) with frequent blood transfusions, the patient being in desperate condition, and three weeks after operation the Friedman test was again negative.

The patient was discharged for further observation, rapidly developed cerebral metastasis and died some five months subsequent to operation.

In reviewing this case it is now obvious that the first curettings which were considered to be deciduitis were in reality chorionepithelioma, and

Again, common sites of metastasis are the vagina and vulva, the mechanism of which has not been satisfactorily explained, although von Recklinghausen attempted it in his theory of retrograde lymphatic transmission. These vaginal metastases are peculiar in that they may not make their appearance for months, although sometimes they are noted even before the primary uterine growth has been discovered. Under such conditions, panhysterectomy will be of no avail.

Tumors composed of fetal cells are markedly under the influence of the gonadal hormones, or, rather, seem to exert a profound effect upon the activity and production of these substances. Hence, it would seem advisable to preserve the regularly recurring cycle of estrin and progestin formation in the hope that by this means, retrogression and absorption of the aberrant fetal elements might be facilitated. Allowing the ovaries to remain, therefore, is worthy of trial. Study of the present series of cases has convinced the writers that much more information may be obtained concerning chorionepithelioma; first, by the systematic histologic examination of hydatidiform moles to ascertain whether or not the piling up of decidual cells in portions of certain of these growths taken in conjunction with the subsequent history of the patient is indicative of potential malignancy; and second, by the intensive study of reasonably large groups of cases which may be accomplished by the pooling of material in the larger cities, and its working up by individuals or committees appointed by local obstetric or gynecologic societies.

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Settergren, F.: The Danger of Infection From Catheterization of the Bladder and Indications for Catheterization in Obstetric Cases, *Acta obst. et gynec. Scandinav.* 16: 202, 1936.

The material comprises 400 cases evenly divided into two groups. In Group 1, each patient was catheterized at least three times before she was discharged from the hospital. No antiseptics were used before the catheter was inserted into the bladder. In Group 2, on the other hand, catheterization was performed only upon definite indications and always under antiseptic precautions. Infections occurred in 29.2 per cent of the first group, and in only 12.2 per cent of the second group. If the presence of pus cells is used as a criterion of infection, the corresponding figures are 20.5 per cent for Group 1, and 5 per cent for Group 2. The author feels certain that the number of urinary infections increased with the number of catheterizations. Only a small number of patients developed subjective symptoms and pyelitis occurred in only one case. Follow-up examinations from two to four weeks after delivery showed spontaneous healing in most instances. The author is of the opinion that urinary antiseptics should be given prophylactically to most women immediately after labor. The author suggests a new way of obtaining sterile specimens of urine after delivery.

J. P. GREENHILL.

presence of persistent fetal elements in uterine scrapings or tissue masses, render the diagnosis of chorionepithelioma practically certain.

On the other hand, when under the same conditions these tests remain negative, one cannot be sure that a chorionepithelioma of low proliferation and malignant quality is not present. Radical surgery is indicated, therefore, whenever persistent fetal elements are found, especially if irregular bleeding is a symptom, regardless of a negative Aschheim-Zondek test.

ANALYSIS OF THE FIFTEEN PHILADELPHIA CASES

	MOLE PRE- CEDING	DIAG- NOSIS BY CURET- TING	OPERATION	FRIED- MAN TEST	OUTCOME
1	Yes	Yes	Panhysterectomy	+ after opera- tion -	Well
2	Yes	Yes	Panhysterectomy	+ after opera- tion -	Well
3	No	Biopsy spec.	Radium and total hys- terectomy	?	Dead of metastasis 6 months
4	Yes	Yes	None	?	Died
5	No	Yes	None	++	Disappeared from view
6	No	No	On laparotomy found in uterus and ovary	++	Died in one month
7	Yes	No	On laparotomy supra- vaginal hysterectomy	+	One year later x-ray showed apparent me- tastasis to kidney. X- ray and radium. Now well
8	Yes	Yes	Supravaginal hysterec- tomy	+	Died four days after op- eration
9	Yes	No	Diag. made from extir- pated uterus	+	Discharged well; lost to view
10	Yes	No	Diag. made from uterus supravaginal hysterec- tomy	+	Radium and x-ray Now well
11	No	No	Radium	?	Died of metastases, few months
12	No	No	Diag. made from extir- pated uterus	++	Radium death from intra- abdominal hemorrhage
13	Yes	Yes	Vag. hysterectomy	--+	Death from metastases 6 mo. later
14	No	Yes	Hysterectomy	?	Dead of peritonitis
15	No	Yes	Radium	?	Now has vesicovaginal fistula, otherwise well

An interesting question arises as to the type of operation which offers the hope of the best results in these cases.

The commonly accepted plan is to perform an extensive pānhysterectomy with removal of both tubes and ovaries.

Since metastasis in chorionepithelioma is generally by way of the blood stream into distant organs, the lungs, brain, and liver being most frequently attacked, whereas secondary growths in the broad ligaments and uterine adnexa are relatively uncommon, it is questionable whether such wide dissection is of any value.

cent of the patients showed a hemoglobin of 70 per cent or less on admission. Treatment of the anemic patient during this period may be the means of combating infection later on.

Instruction of the patient should stress the importance of a well-balanced diet with emphasis on such food elements as iron, calcium, and the vitamins. Excessive gain in weight should be controlled, since this leads to undue strain which becomes reflected in the patient's general condition at term. An average gain of about 18 pounds is considered ideal. The patient should also be instructed regarding the hygiene of pregnancy. Douching is permitted only under instruction. Coitus is not permissible during the last few months. The importance of coitus as a means of introducing virulent organisms into the vagina just before the onset of labor cannot be accurately determined, but our attention has been called to several cases in which this may well have been the etiologic mechanism. In addition to such instructions as outlined above, the patient should be given a list of reportable symptoms among which should be included the rupture of the membranes. In any case history study of puerperal sepsis there will be found a group that started as antepartum infections of the amniotic sac. Characteristically, these patients, when entering the hospital early in labor, give a history of having ruptured the membranes three or four days before, although they did not think it important enough to report. An examination may reveal the escape of a small amount of amniotic fluid which, as the infection progresses, may become purulent in character. Labor is most often characterized by poor contractions, and by the time the patient is delivered, or shortly thereafter, there is a sharp rise of temperature which may be preceded by a chill. Fortunately, in most instances, the temperature subsides as soon as the uterus obtains its natural drainage following delivery, and the patient gets better, but there are others who develop a spreading sepsis which may end fatally. During the past eight years we have seen three such fatalities.

CONTROL DURING LABOR

The first point under this heading deals with the routine nose and throat cultures of the labor room staff. All new students and nurses, as well as the doctors, are cultured for the hemolytic streptococcus. Carriers are excluded from duty until repeated cultures prove negative. The nurses' duties are confined entirely to the obstetric division of the hospital during the period of training, thus avoiding contact with the cases in the medical and surgical wards.

The second point refers to the routine vaginal cultures of the patients for the same organism. During the past three years in the course of several thousand such cultures, we have noted an incidence of 3.4 per cent positives. These patients are isolated as will be described later on. Although they do not seem to show a much higher incidence of infec-

THE CONTROL OF PUERPERAL SEPSIS IN HOSPITAL PRACTICE*

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INFECTION of the puerperal uterus constitutes one of the most important complications with which the obstetrician is confronted. The figures on maternal mortality due to sepsis are becoming commonplace knowledge. Even the lay press defiantly waves them before us. This press, poorly guided as it has always been concerning medical subjects, taunts us with the utopian idea that, since puerperal sepsis is a preventable disease, we should make it our job to wipe it out in much the same way as has been done with typhoid fever or diphtheria. Needless to say, the problem with puerperal sepsis is quite different, and for the present, at least, we will have to content ourselves with the fact that a certain amount of sepsis will be inevitable. There is no doubt, however, that the present high incidence of this complication could be materially lowered, and it is toward this end that this plan of control is offered. The various features of the plan have formed the guiding principles of practice at the Sloane Hospital for Women for the past eight years and are largely an embodiment of the ideas along these lines of our director, Dr. Benjamin P. Watson. A general program of control should include not only the measures aimed at the direct prevention of sepsis, but also the management of the patient with the purpose of conserving her resistive forces, so that in the face of an acquired infection she will more effectively combat it.

The subject may be divided under the following headings:

- (1) Control during the antepartum period
- (2) Control during labor
- (3) Control during the puerperium

CONTROL DURING THE ANTEPARTUM PERIOD

The measures which can be profitably employed during this period are largely designed to build up the resistance of the patient. The patient is given a complete physical examination when she first comes to the clinic. A careful examination will often reveal disease processes complicating the pregnancy, which will require special handling during the antepartum period in order that the body resistance can be maintained at as high a level as possible. A routine estimation of the erythrocyte count and hemoglobin is most important. In our clinic about 9 per

*Read before the Section on Obstetrics and Gynecology, New York Academy of Medicine, May 26, 1936.

sis on the type of antiseptic used to prepare the skin is not desirable, because it detracts from the importance of other more important features of the technic.

The fifth point deals with vaginal examinations during labor. We believe that a vaginal examination carries no greater risk of infection than a rectal examination, if it is carefully done. The doctor prepares himself and the patient in exactly the same way as he does for the delivery, including the change to operating room clothes and shoes, cap, mask, sterile gown, and gloves. The only exception we make is that for the vaginal examination the sterile field is made smaller. The examining fingers are introduced directly into the vagina without making contact with the vulvar surfaces. If the technic of the vaginal examination is not as good as that employed for the actual delivery, then it is obvious that the technic of the delivery becomes as bad as that used for the vaginal examination.

The sixth point refers to the technical skill and the judgment used in carrying out obstetric procedures. In this category we feel that the following are very important considerations:

1. Make an early appraisal of the prognosis of labor in order to avoid the dangers of the late cesarean section. In spite of all the recent refinements of surgical technic, the late cesarean section carries a high maternal mortality from sepsis. The low flap operation has given us better results than the classical operation so far as infection is concerned, but neither this nor the Latzko type of extraperitoneal cesarean section is a safe procedure in the face of uterine infection.

2. Carry out obstetric operations on defensible indications in order to avoid unnecessary and untimely instrumentation and subsequent trauma. Traumatized tissue has a lowered resistance and therefore favors the activation, invasion and final spread of organisms already present in the vagina, leading to an endogenous type of infection, usually by anaerobic bacteria.

3. Handle the third stage with great care in order to avoid hemorrhage. Excessive loss of blood breaks down the defense mechanism, the only means of cure at the patient's disposal.

4. Repair all lacerations properly.

CONTROL OF SEPSIS IN THE PUERPERIUM

This phase of the problem is concerned with two main points: (1) Nursing care in the puerperium. (2) The isolation of infected or potentially infected patients.

With respect to the nursing technic the following are the main points upon which it is based:

1. The nurse masks the nose and mouth before she does a perineal dressing.
2. She scrubs her hands and arms for two minutes before giving such care.
3. The major part of the equipment used for the care of the perineum is individual for the patient.
4. All equipment that is not individual is sterilized.
5. Complete q-4 hours temperature readings are recorded.

tion than the noncarriers, the morbidity rates of the two groups being 12.2 per cent for the carriers and 7.8 per cent for the noncarriers, we isolate them because we feel that the organisms they carry may be virulent for their neighbors. Until the technic of Lancefield or Hare, by which streptococci can be classified, is applicable to routine clinical work, carriers among the staff and patients will have to be considered potential sources of infection.

The third point concerns the reduction of contacts in the labor room. About three years ago we adopted a contact sheet on which each person who made any physical contact with the patient in labor had to write his or her name. The purpose of keeping such a list was to enable us to make a search for a possible carrier among these contacts when a patient developed an infection. When we started the contact sheet, we were much surprised to find that some patients were handled in one way or another by as many as twenty-five different people. Needless to say, this number has been considerably reduced. It seems only natural to believe that the reduction of such contacts lessens the possibilities for exogenous infections.

The fourth point deals with asepsis. The routine consists of a change from street or hospital clothes and shoes to operating room wear. A cap and a 4-ply gauze mask placed over the nose and mouth complete the dress. We emphatically stress the importance of placing the mask over both the nose and mouth. This is followed by a five-minute scrub of the hands and arms with green soap in running water, alcohol rinse, and sterile long-sleeved gown and gloves. The patient is then prepared with half-strength tincture of iodine. The prepared field includes the vulvar inner aspects of thighs, the suprapubic area and, last, the anal region. The field is then draped with sterile towels, sheets, and leggings. Before the examining fingers are introduced into the vagina, the labia are carefully separated and the vaginal orifice is swabbed with several pledgets of cotton that have been soaked in a 1 per cent lysol solution. The fingers are then introduced directly into the vagina without touching the vulvar skin surfaces. By carrying out the examination in this way, there is little possibility of introducing organisms from the outside into the vaginal canal. We are not much concerned with the particular virtues of the various antiseptics used to prepare the sterile field. It is quite probable that soap and water would do just as well. It is noteworthy that a particular clinic will often change the type of antiseptic after a series of infections have occurred. In addition to this change, various other modifications are made in the technic which, consequently, make everyone infection conscious and result in greater vigilance and care in carrying out the details of the plan. Then, strange as it may seem, when the morbidity rates are studied, all the credit for the more recent lower rate is given to the new antiseptic. Too much empha-

SECONDARY PERINEORRHAPHY AT A SUBSEQUENT DELIVERY

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THE immediate repair of perineal injuries incident to delivery has become generally accepted obstetric practice, but it is not yet widely recognized that the unsatisfactory results of previous obstetric trauma, with or without attempted early repair, may be attacked surgically at the time of a subsequent delivery. This report summarizes the results obtained in such secondary repairs of the perineum performed in the University Hospital from July 1, 1926 to Dec. 31, 1934.

Apparently, Bubis,¹ in 1925, first called the attention of the profession in this country to the practicability of repairing old vaginal and cervical lesions at the time of a subsequent delivery and refuted the older ideas that such attempts were unwise because of the edema and friability of the tissues and because the lochial discharges would interfere with healing. His records indicated that the results to be expected were as good as, or better than, those obtained from the more routine surgical attack upon such lesions during an interval between pregnancies. During the past decade, Bubis has elaborated his hypothesis and has received support from the majority of obstetricians who have attempted his technic, although an occasional statement of disagreement has appeared. Before the appearance of Bubis' communication, a small independent experience in the same direction had demonstrated the validity of his conclusions, and it has, therefore, been the practice in the clinic to subject those patients, who show old, symptom-producing perineal relaxations, to immediate postpartum repair, provided no contraindication exists.

The technic of the operation, which is performed immediately after expulsion of the placenta, does not differ from that followed in other secondary repairs, but allowance must be made for subsequent involution. No variations in the usual postpartum care are necessary, except that, after repair of a complete laceration, evacuation of the bowels should be postponed for several days, during which a low residue diet is given.

During the years under consideration, 4,412 patients were delivered, including 1,965 primigravidas and 2,447 multigravidas. Among the

The fundamental idea, therefore, upon which the nursing care of the puerperium is based, is that of prevention of infection from the nose, throat, and hands of the nurse to the patient, and of the prevention of infection from one patient to another.

The isolation of infected patients, carriers, and unregistered cases we consider a most important part of the general plan of control. The isolation unit is virtually a small, complete hospital within the main hospital. It can function with complete independence from the main service, since it is equipped with its own pantries, nurseries and delivery-operating room. To this unit are sent all patients who show any evidence of infection, regardless of the cause. Here they are received in an observation ward until a definite diagnosis is established. Cases of puerperal sepsis are further isolated in a smaller ward within the unit especially reserved for them. All patients in the isolation unit are separated by individual cubicles and are handled according to a technic patterned after that in common usage in contagious hospitals. In this way each patient becomes an entirely separate unit, thus eliminating the possibility of cross infections. This last point needs emphasis. If the isolation unit has no provisions for avoiding cross infections, then there will necessarily be great hesitancy about sending the mildly infected case to this unit. Certainly one would hesitate to send a patient with a simple upper respiratory infection to such an unprotected unit. By using the technic described, the patient has practically complete security from cross infections, and we do not hesitate to transfer even normal puerpera to this unit. Normal women, incidentally, who are nursing their babies, may be transferred there with their babies when the latter require isolation. We have not a single recorded instance of an acquired cross infection in this normal group during eight years of operation.

We conclude from this more or less categorical exposition of the subject that prophylaxis against puerperal sepsis is a battle that must be fought on many different fronts. There are no short cuts. It is a battle that requires an organized effort on the part of all, an insistence on uniformity of methods, a loyalty of purpose and, finally, a repetition of details that becomes ritualistic and automatic in performance.

Yuki, S.: Another Death of a Fetus After the Administration of Quinine, *Jap. J. Obst. & Gynec.* 19: 311, 1936.

The author reports a case of a woman who was given 3 gr. of quinine at 2, 4, and 6 o'clock. She was not in labor. The next morning the patient complained that she could not feel fetal movements. Auscultation failed to reveal the heart tones which had previously been heard. Uterine contractions set in shortly and a still-born child was born. In a case reported by the author in 1934 autopsy revealed changes in the liver and kidneys which could be regarded as having been due to intoxication from quinine.

J. P. GREENHILL.

TABLE I. REPAIRS OF INCOMPLETE PERINEAL LACERATIONS IMMEDIATELY AFTER A SUBSEQUENT DELIVERY

TYPE OF OPERATION	NO. OF PATIENTS	AVER. NO. OF DAYS IN HOSPITAL AFTER OPERATION	MORTALITY	MORBIDITY		RESULTS	
				ONE-DAY FEVER	MORE THAN ONE-DAY FEVER	ANATOMICAL	FUNCTIONAL
Perineorrhaphy	128	12.1	0	12 9.3%	3 2.3%	Good* 124 Fair 4	Good 128
Perineorrhaphy and anterior colporrhaphy	6	13.5	0	3 50.0%	0 0.0%	Good 6	Good 6
Perineorrhaphy, anterior colporrhaphy, and cervical repair	3	14.8	0	2 66.6%	0 0.0%	Good 3	Good 3
Perineorrhaphy and cervical repair	2	13.0	0	1 50.0%	1 50.0%	Good 2	Good 2
Total	139	12.2	0	18 13.0%	4 3.1%	Good 135 Fair 4	Good 139

*Good, satisfactory
Fair, not completely satisfactory, but not a real failure.

TABLE II. REPAIRS OF COMPLETE PERINEAL LACERATIONS IMMEDIATELY AFTER DELIVERY AS COMPARED WITH SIMILAR OPERATIONS MONTHS OR YEARS AFTER THE LAST PRECEDING PREGNANCY

TIME OF OPERATION	NO. OF PATIENTS	AVER. NO. OF DAYS IN HOSPITAL AFTER OPERATION	MORTALITY	MORBIDITY		RESULTS	
				ONE-DAY FEVER	MORE THAN ONE-DAY FEVER	ANATOMICAL	FUNCTIONAL
Immediately after delivery	22	14.3	0	3 13.6%	1 4.5%	Good* 19 Fair 3	Good 21 Poor 1
Months or years after last preceding delivery	60	17.1	1 1.7%	23 38.3%	12 20.0%	Good 44 Fair 12 Poor 4	Good 52 Fair 6 Poor 2

*Good, satisfactory
Fair, not completely satisfactory
Poor, failure

latter group, 161 secondary perineal repairs were performed, an incidence of 0.66 per cent. The operations included:

Repair of old complete perineal lacerations	22
Repair of old incomplete perineal lacerations	128
Repair of anterior and posterior vaginal walls	6
Repair of anterior and posterior vaginal walls and cervix	3
Repair of posterior vaginal wall and cervix	2
	<hr/> 161

The results of immediate postpartum repairs of old complete tears were compared with those obtained in a consecutive series of secondary repairs of similar lesions on the gynecologic division, where the same technic, performed by the same group of operators, and the same after-care were employed, but where the patients were some months or years removed from the last preceding pregnancy.

Convalescence was judged by the postoperative temperature response according to the following criteria: Mouth temperatures were recorded every four hours, day and night during the patient's stay in bed, and temperatures of 100.4° F. or more were considered abnormal. A diagnosis of "febrile morbidity" demanded that the temperature rise to 100.4° F. or more on any two days after operation, excluding the first twenty-four hours.

Final operative results were judged by two standards: (a) Visual and palpable evidence of proper healing, and (b) the functional capacity of the repaired structures as indicated by the patient's relief from previous symptoms.

RESULTS

Simple Repair of Old Incomplete Perineal Lacerations.—One hundred and twenty-eight patients were subjected only to secondary perineorrhaphies immediately after delivery (Table I). The hospital stay was hardly prolonged above the average for patients who had recent lacerations repaired. There was no mortality and the total febrile morbidity, 11.7 per cent, was actually lower than the average for the clinic when the same criteria are employed. In four instances, 3.1 per cent, primary healing did not occur, but the final functional result was invariably good.

Repair of Old Incomplete Perineal Lacerations Associated with Other Plastic Repairs.—In eleven patients, perineorrhaphy was accompanied by the plastic repair of other injuries from preceding deliveries (Table I). It will be noted that there is a high incidence of one-day elevations of temperature (55.0 per cent); but that the puerperium was "febrile" in only one instance (9.0 per cent). The repairs all healed satisfactorily and the functional results were good (Table I).

Repair of Old Complete Lacerations.—During the interval reviewed, twenty-two complete tears sustained at some previous confinement were repaired immediately after delivery on the obstetric division, while the same operators, using identical operative technics and similar after-care on the gynecologic division, attacked sixty complete tears some months or years after the last preceding pregnancy (Table II). The advantages of repairing such old complete tears just after another delivery are reflected in the lower morbidity among the first group, as well as in the higher percentages of satisfactory anatomic healing and of functional restoration.

CONGENITAL HYDROPS FETALIS (SCHRIDDE TYPE)*

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THE birth of a baby presenting the picture of universal edema is not a new phenomenon, according to reports in the literature going back to the seventeenth century. Its association, however, with a definite blood picture, regular appearing changes in the hematopoietic centers and the finding of extramedullary centers of hematopoiesis is comparatively new. Ballantyne¹ of Edinburgh in 1902 gave a classic description of the condition as he found it and defined it as "a morbid condition of the fetus characterized by general anasarca, by the presence of effusions in the peritoneal, pleural and pericardial sacs, usually by edema of the placenta, and it results in the death of the fetus or infant before, during, or very soon after birth."

Schridde² in 1910 found in the cases where there was no anatomicopathologic basis for the edema that there was a consistent finding of an erythroblastosis in the blood, a stimulation of the hematopoietic centers both intra- and extramedullary, and deposits of hemosiderin in some of the viscera, notably the spleen, liver, and kidneys. He considered the condition as the result of an anemia caused by some unknown toxin, probably arising in the fetus.

Baby C., female, premature seven months, stillborn Sept, 11, 1935. The mother, para iv, thirty-four years old, of French-Canadian extraction, married eight years. No living children at present. The first baby, male, born spontaneously, lived to be four years old and died of what was diagnosed as purpura hemorrhagica. From the description of this baby's last illness the diagnosis was undoubtedly correct. The second pregnancy in 1932 ended in spontaneous abortion at two months. The third pregnancy terminated in 1933 was an intrauterine stillbirth. No autopsy. A personal communication from the physician who delivered her stated that the fetus had died a week or ten days previous to delivery and that it showed no signs of edema but was the typical macerated fetus with which we are all familiar.

Present pregnancy: Last normal period Feb. 9, 1935. Expected date Nov. 16, 1935. First seen by the senior author April 24, 1935, with a history of considerable nausea and vomiting but not persistent enough to be classed as pernicious. Considerable headache and dizziness at times. No edema. Wassermann negative. During May and June she was better under careful diet and attention to the emunctories. During July and August much better, quite normal. Fetal life was first felt about the middle of June. Blood pressure during these months varied from 100/70 to 114/70. Urine normal.

About September 1, she began to complain of asthenia, headaches, dizzy spells, edema of the lower extremities and oliguria. Abdomen steadily enlarging. Only one fetal heart heard. Blood pressure rose fairly promptly to 140/96. Urine showed an increase of albumin but no casts. She was put to bed, diet restricted, low protein and salt free. Saline cathartics each morning. This was tried for one week with no regression of the signs or symptoms. Blood pressure increased to 156/106. General condition less favorable. Pressure of the large uterus increasing the dyspnea. On September 9, she was sent to the hospital for induction of labor. Vaginal examination at this time showed the cervix two fingers dilated with the presenting

*Read before the Eastern New York Obstetrical Society, December 5, 1935.

The one fatality, E. E., Hospital No. A-6472, among the sixty "interval" repairs done on the gynecologic division, was probably due to pulmonary embolism. Autopsy was not permitted, but death occurred on the twelfth postoperative day within thirty minutes after a sudden attack of dyspnea associated with an imperceptible pulse and other evidence of shock, following a mildly febrile operative convalescence.

DISCUSSION

Such results indicate that the older theoretical objections to plastic restoration of the pelvic structures immediately after delivery are unsupported by actual experience and that the probability of satisfactory healing is actually improved at this time. Technically, the performance of perineorrhaphy is simpler by reason of the partial, natural separation of the structural planes and the relaxation of the perineal tissues, while the postpartum hyperemia of the tissues apparently promotes primary union. On the other hand, cystocele repair may be complicated by considerable oozing and by unusual friability of the tissues, making satisfactory closure more difficult; for this reason it should be attempted only by those familiar with pelvic plastic surgery. It should, moreover, be unnecessary to insist that some experience in the usual secondary repair procedures is essential to good results from any gynecoplastic surgery.

SUMMARY

In secondary perineorrhaphy performed immediately after a subsequent delivery, the obstetrician has available a procedure, which (1) is technically simple, (2) gives more generally satisfactory results than do similar operations performed some time after the last preceding pregnancy, (3) is economically advantageous for the patient because it avoids a separate hospitalization solely for the repair, and (4) usually does not complicate convalescence nor increase appreciably the duration of postpartum hospitalization.

It is, therefore, recommended for consideration by those who are familiar with the surgical principles involved in the repair of perineal lacerations and relaxations.

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- (1) *Bubis, J. L.*: AM. J. OBST. & GYN. 10: 213, 1925.

Hauch, B., and Moller-Christensen, E.: Preliminary Results With Ergometrine, Acta obst. et gynec. Scandinav. 16: 152, 1936.

Studies made by these authors convinced them that Moir's claims are justified. They found that better results were obtained with ergometrine than with corresponding doses of fluidextract of ergot.

J. P. GREENHILL.

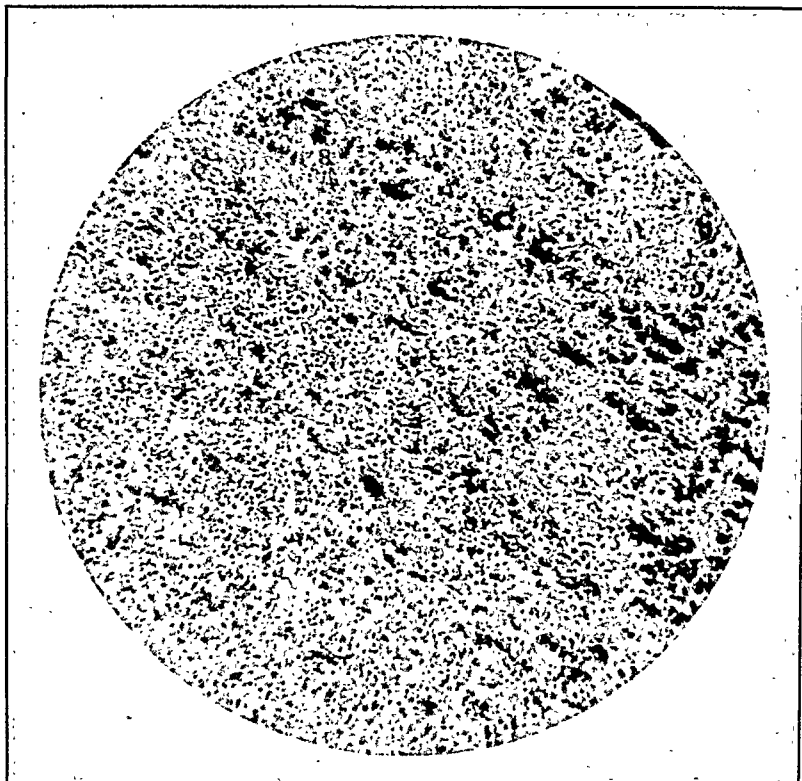


Fig. 1.—Marked diffuse hemopoiesis of liver. Dark granules in hepatic cells represent hemosiderin. $\times 120$.

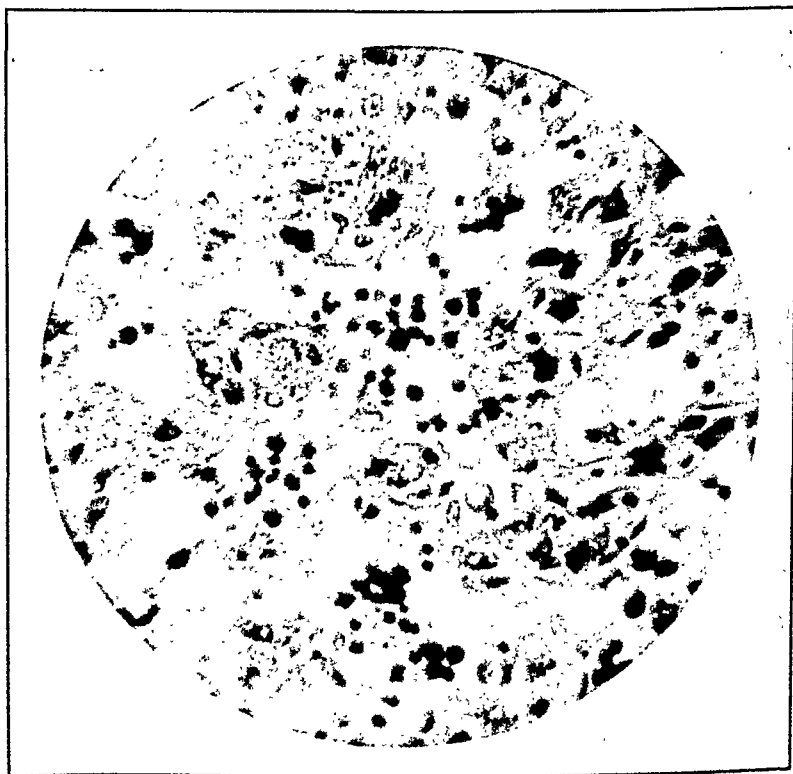


Fig. 2.—Numerous megaloblasts and normoblasts between reticulum lining and hepatic cell cords and in liver sinusoids. Note amitotic division of nuclei in some of the normoblasts. $\times 500$.

part fairly high above the brim. It could not be definitely determined whether a deformed head or the breech was in the cervix. Abdominal examination was unsatisfactory on account of the tense uterus. Fetal heart present, 140 per minute. Hydramnios with anencephaly was suspected. Patient was given 10 c.c. of 25 per cent magnesium sulphate intramuscularly every four hours; a milk diet and a retention enema of chloral and bromides were given for sleep. Twenty-four hours after admission the membranes were ruptured and a definite breech made out in the cervix. Blood pressure at this time 160/100. Labor started promptly at 2 P.M. September 10. Delivery of a stillborn edematous fetus, placenta, and cord occurred at 9:36 A.M. September 11. Fetal movement had stopped about 9:30 P.M. on the tenth, and no fetal heart could be elicited thereafter. Two specimens of urine taken while the patient was in the hospital showed traces of albumin with many granular casts on one occasion and only an occasional cast on the second test.

The postpartum convalescence of the mother was quite normal. Urine output increased, edema disappeared, blood pressure came down slowly so that on the twelfth day it was again 110/80. When the patient returned for her six weeks examination, the blood pressure was 116/80, no edema, and urine normal. Her only complaint was moderate asthenia. Blood count showed a moderate secondary anemia.

COMMENT

While the first-borns are usually spared from these blood dyscrasias, from the outcome of the first baby in this case followed some time later by another showing definite signs of erythroblastosis, I wonder if the first-born might not have been one of the cases of congenital anemia or erythroblastic anemia which eventually became purpuric.

Autopsy.—Gross and microscopic description. The body was that of a premature stillborn infant, having a crown-rump measurement of 27 cm., indicating a fetal age of about seven months. A large edematous placenta weighing 900 gm. and an umbilical cord 130 cm. in length were attached. There was an extremely marked generalized edema of the subcutaneous tissues. The soft tissues of the face were swollen, compressing the eyelids. The labia were tense with fluid. Large ecchymotic bullae were present over the lower extremities. The peritoneal cavity contained about 250 c.c. of clear serous fluid and each pleural cavity about 75 c.c. The pericardial fluid was not excessive.

The heart was of normal size and shape. The myocardium was firm and dark red. The foramen ovale and ductus arteriosus were patent. The lungs were atelectatic. The liver and spleen were moderately enlarged. The hepatic parenchyma was dark red and the lobules indistinct. The splenic pulp was soft and homogeneously red. The kidneys appeared congested. The thymus gland was smaller than normal. The medulla of the femur was filled with soft red cellular marrow.

Histology.—*Liver:* (Figs. 1 and 2.) The principal histologic findings in the liver were marked erythroblastosis and very heavy deposition of hemosiderin pigment. Diffuse hemopoiesis was observed between the reticulum lining the liver capillaries and the cords of hepatic cells. The majority of the blood cells were megalo-blasts and normoblasts. The former presented large vesicular basophilic nuclei containing nucleoli with a narrow rim of clear neutral cytoplasm. The normoblasts exhibited small round hyperchromatic nuclei with a rim of light blue to brown cytoplasm. Several of the cells were undergoing nuclear division. Small numbers of various types of myeloid cells were scattered among the erythropoietic tissue. The liver cords were shrunk as though by pressure of the adjacent hematopoietic cells. The cytoplasm of the hepatic cells was heavily laden with brown pigment which gave the Prussian blue reaction for hemosiderin. The reticulo-endothelial cells contained little demonstrable pigment. The sinusoids were dilated and the blood in them showed many primitive nucleated cells.

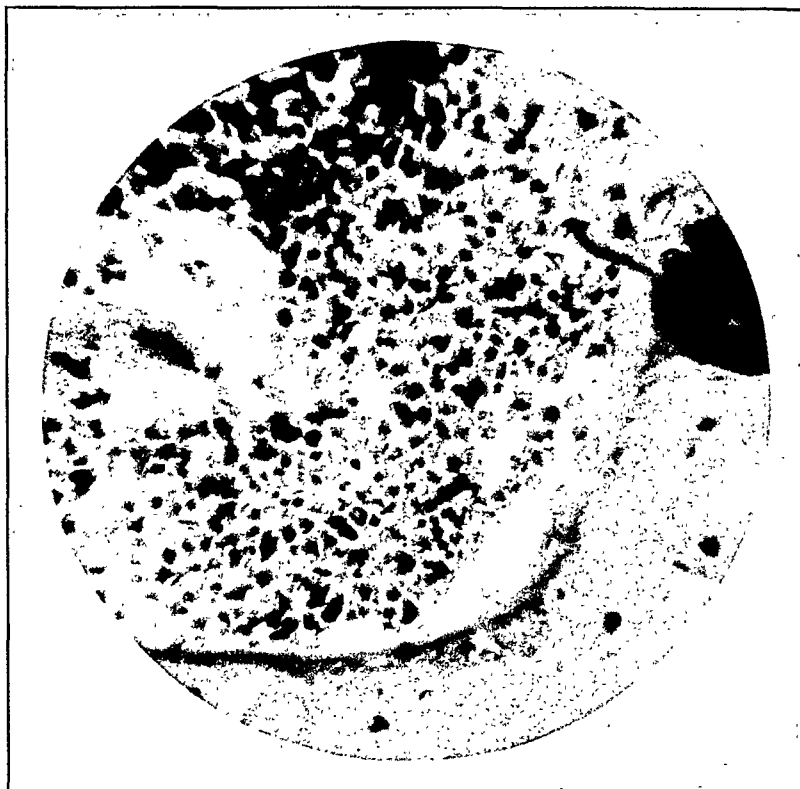


Fig. 4.—Bone marrow (femur). Marked hemopoiesis, chiefly erythrogenic. $\times 500$.

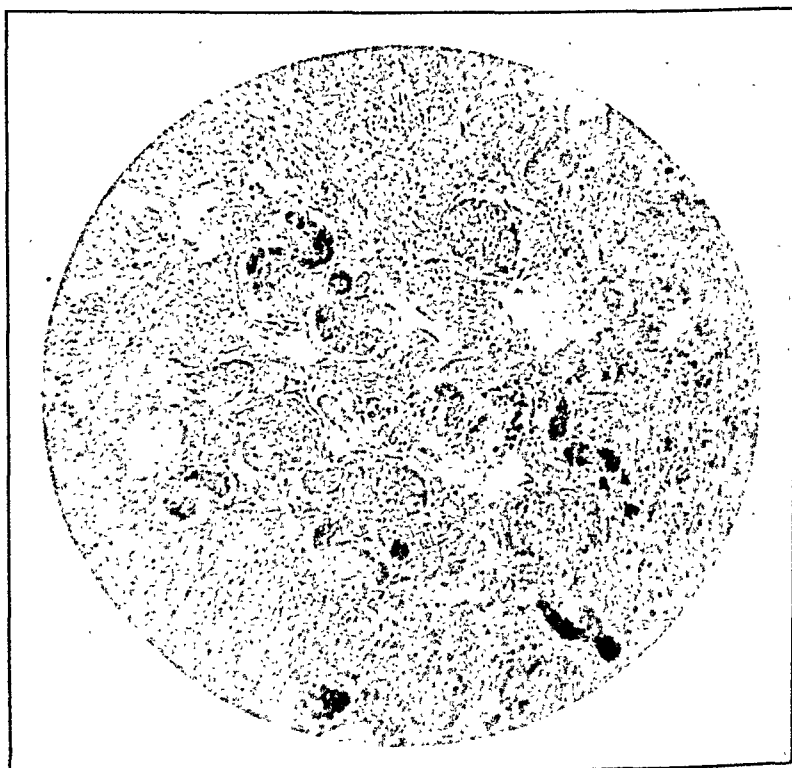


Fig. 5.—Large amounts of brick red granular pigment (hemoglobin) in H&E-stained cells of renal tubules. The pigment appears as closely packed black granules in this microphotograph. $\times 120$.

Spleen: (Fig. 3.) The spleen showed diffuse hemopoiesis, the predominating cells being erythropoietic. Lymph follicles were not present. The splenic reticulum was prominent and the sinusoids appeared distended. Many of the reticulo-endothelial cells were enlarged and filled with brick red pigment which failed to give the Prussian blue reaction for iron. It was considered to be hemoglobin.

Bone Marrow (Femur): (Fig. 4.) The spaces between the bone trabeculae were filled with blood cells, chiefly erythrocytic. Normoblasts, erythrocytes and megakaryocytes composed the marrow in about the order named, with a few intermingled myeloid cells, megakaryocytes and lymphocytes. Free blood pigment was not demonstrable here.

Kidneys: (Fig. 5.) The architecture of the kidneys was of the fetal type with large hyperchromatic glomerular tufts and a moderate amount of loose interstitial tissue, particularly noticeable in the medullary portions. The striking finding was

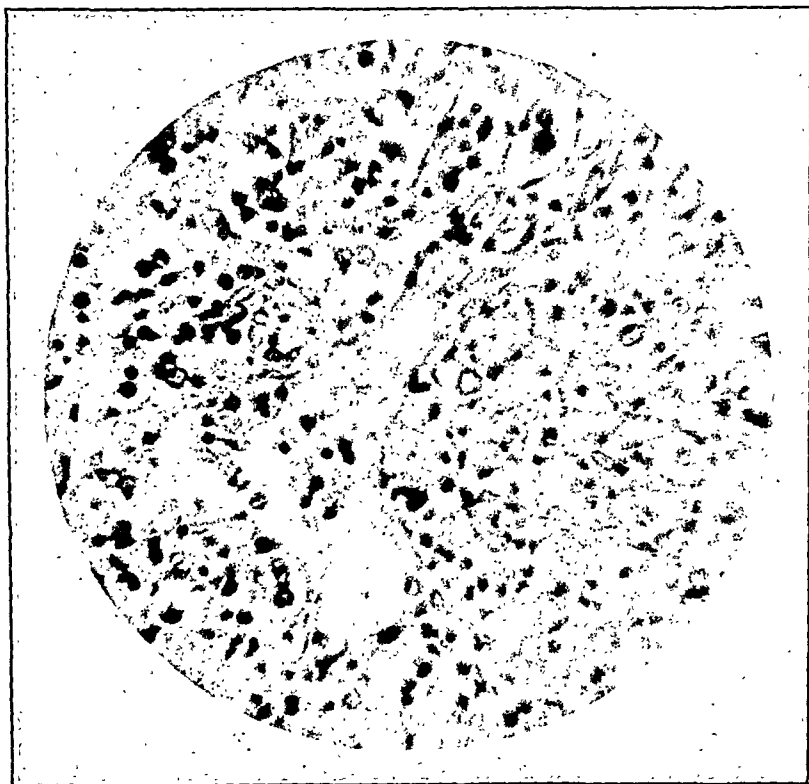


Fig. 3.—Spleen. Note enlarged reticuloendothelial cells and many nucleated erythrocytic cells. $\times 500$.

the presence of large amounts of brick red granular pigment in the lining cells of the convoluted tubules. This pigment like that in the spleen proved to be hemoglobin. A few of the smaller collecting tubules contained hyaline casts.

Blood Smear (Umbilical Cord): (Fig. 6.) A Wright's stained smear of blood collected from the cord vessels at the time of delivery revealed 11 per cent megakaryoblasts, 17 per cent normoblasts, and 72 per cent erythrocytes among 500 cells of the erythrocytic series. Leucocytes were very rare. Of those present, about 65 per cent were lymphoid and 35 per cent myeloid.

Other Tissues: The lungs showed atelectasis. Erythropoietic cells, principally intravascular, were observed in all of the organs. A section of abdominal skin (Fig. 7) showed marked edema of the subcutaneous tissue with small focal hemorrhages. The placenta exhibited edema of the connective tissue in some of the chorionic villi.

Pathologic Summary.—Marked generalized anasarca, blood pigment deposition, and erythroblastosis. The blood pigment predominated in the liver as hemosiderin and in the lining cells of the convoluted renal tubules as well as the reticulo-endothelial cells of the spleen as hemoglobin. Erythroblastosis was strikingly present in the bone marrow, the liver and the spleen. The heart, thymus gland, lymph nodes, kidneys, lungs, skin, and circulatory blood contained erythropoietic cells.

DISCUSSION

The presence of erythroblastosis may be suggested by the finding of generalized anasarca, icterus or anemia in a newborn infant. The demonstration of a high percentage of nucleated cells of the erythrocytic series in a smear of blood from the infant or the umbilical cord is a reliable confirmatory test. Recent studies made at the Bender Hygienic Laboratory in which umbilical cord smears were examined from 59 normal cases showed in each instance less than 0.5 per cent of the erythrocytic cells to be nucleated. Megaloblasts were practically absent and in most of the smears normoblasts were encountered rarely. This is in sharp contrast to the cord smear in the case presented in which 28 per cent of the erythrocytic cells were primitive nucleated ones. The wide dissemination of erythroblastosis in various body tissues studied at necropsy indicates that this was an important feature of the disease.

We have mentioned several theories that have been postulated concerning the nature and etiology of erythroblastosis in the newborn. However, none of these explain why in some cases anasarca is strikingly prominent, in others icterus and in still others anemia. May we offer the following hypothesis for consideration.

Erythroblastosis with anasarca develops during fetal life, the afflicted only occasionally progress to term and have never been known (reported) to live more than six days after birth. Apparently the destruction and excessive production of erythrocytes is very deleterious when it occurs in early fetal life. Perhaps the deposition of hemoglobin in the renal epithelium and the continued effort to excrete this pigment may impair developing kidneys with resultant damming back of fluid excretion.

If the condition develops later in intrauterine life, the fetal kidneys are better prepared to perform their task. However, if the erythroblastosis and destruction of erythrocytes progress to a fulminating degree, the patient will develop severe jaundice and succumb to icterus gravis.

The cases of congenital anemia (Cooley's anemia) which have been classed in this group are of a much milder nature than those exhibiting anasarca or icterus. They are often apparently normal full-term infants who develop marked pallor and anemia, some times with slight jaundice several days after birth. Most of these patients recover. As the erythroblastosis and destruction of blood corpuscles occur relatively late in life, we would expect the infant to more successfully cope with the disease.

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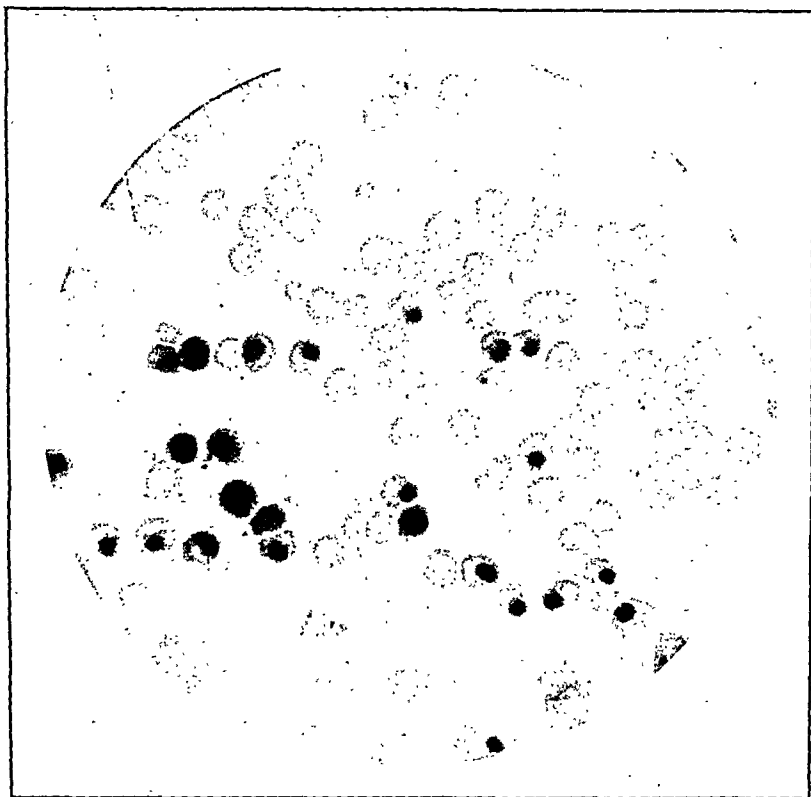


Fig. 6.—Blood smear (umbilical cord) showing high percentage of erythropoietic cells. The cells with large nuclei and little cytoplasm are megaloblasts; those with small round nuclei and much cytoplasm, normoblasts. Intermediate forms may be termed erythroblasts. $\times 500$.

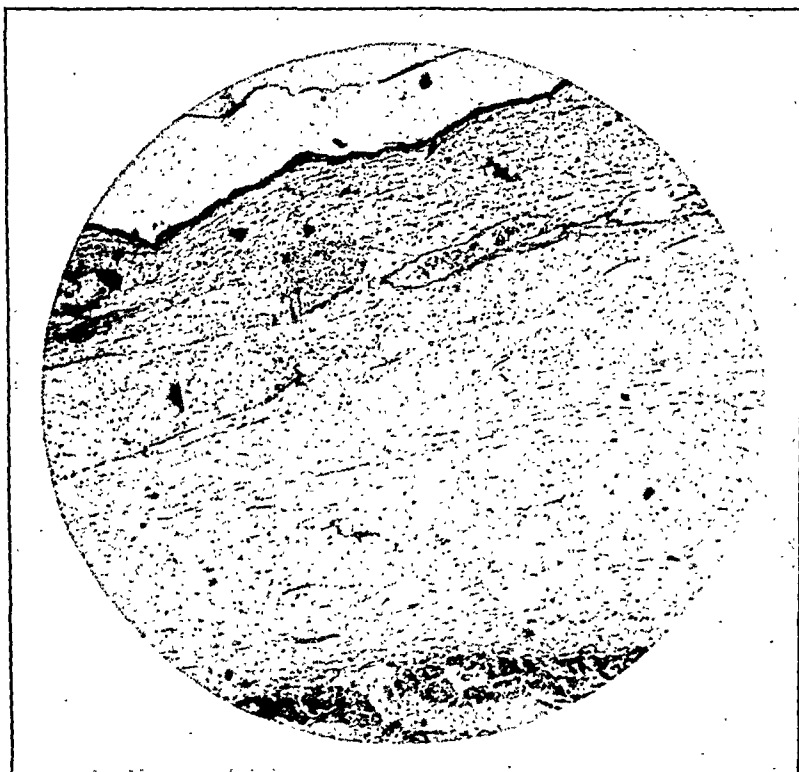


Fig. 7.—Abdominal skin. Marked edema of subcutaneous tissue with small focal hemorrhages. $\times 50$.

Microscopic Examination.—(a) Tissue was covered by single layer low columnar cells, showing very slight infolding. Underlying glands were rather numerous; they varied considerably in size and shape, many being small and round and others showing slight cystic dilatation. Glands were lined by single layer low columnar cells; in some areas this epithelium was quite edematous. Supporting stroma was moderately dense and in most of the section showed considerable edema. Numerous lymphocytes were seen throughout the stroma (Fig. 1). (b) Stroma was dense and fibrous; in many areas it was quite edematous. Blood vessels were engorged. Numerous corpora albicantia were seen throughout the stroma. For most part the ovary was replaced by rather solid masses of tumor cells which were small and deep staining, resembling granulosa cells of normal follicle. The cells were compactly arranged and showed little variation in staining properties; occasional mitosis was seen. In some areas small glandlike or cystic spaces were noted lined by single layer small cuboidal cells; this layer of epithelium was directly supported by the tumor cells. The cells invaded the stroma in many places; in more solid areas fine fibrous

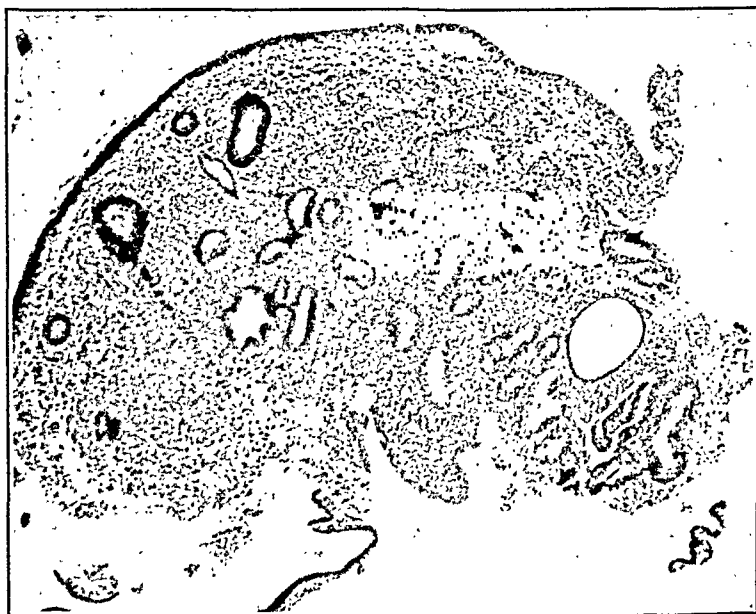


Fig. 1.—Microphotograph of endometrium showing moderate hyperplasia.

connective tissue stroma was seen. Other sections showed larger cystic areas similar to those described, in which considerable necrosis and degeneration were noted. In some places normal ovarian stroma was markedly edematous and contained considerable extravasation or red blood cells along with hemosiderin deposits (Figs. 2 and 3).

Diagnosis.—(a) Glandular hyperplasia of endometrium. (b) Granulosa cell tumor, left ovary.

This patient was seen again on April 15, 1935. Her operative incision was well healed. There was no evidence of recurrence of the tumor. The uterus was extremely small. She was last seen on Feb. 26, 1936. No change was found as compared to her previous visit. She stated that she was having marked hot flashes and was extremely nervous. She had never experienced these symptoms before although her menopause had occurred at the age of forty-four years.

In view of marked sensitivity of the follicular system to radium therapy, the use of this form of treatment is immediately suggested in the granulosa cell tumor. This case, therefore, is of considerable interest. At a stage when the tumor was too small to be easily detected clinically, radium therapy was utilized. The rup

RADIUM THERAPY IN GRANULOSA CELL TUMOR OF THE OVARY

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RECENTLY in listening to a general discussion of ovarian tumors by Pemberton,¹ a patient with a granulosa cell tumor was mentioned, who, unfit for operation, was receiving radium therapy. The speaker stated that he had been unable to find any information on the effect of radium on these tumors. Novak and Brawner² state that few reports have been made on this form of treatment. In view of this, it was felt that the following case would be of interest.

Mrs. G. M., aged sixty-seven years, widow, para ii, gravida ii. Menopause at forty-four years of age. No bleeding until present history. No menopausal symptoms. On June 7, 1933, she had vaginal bleeding which persisted for a month. The patient was treated by Dr. Charles Larkin of Waterbury, Conn. He performed a curettage and cauterized several nabothian cysts. Following this 100 mg. of radium were placed in the uterus and left for thirty hours. Sections of these curettings showed hyperplastic endometrium with no evidence of malignancy. At the time of the operation there was noted a small fibroid on the right side of the fundus. No further bleeding occurred, but on return to Dr. Larkin on June 26, 1934, he found a cyst of the left ovary which was described as being about the size of an orange. He noticed at the time that the uterus was small and in good position. He advised operation but the patient ignored this advice. She was seen for the first time by the author on March 1, 1935, when she stated that she had been bleeding for about one month.

The patient was an elderly female who appeared in excellent condition. General physical examination negative except for slight thickening of brachial arteries.

There was an elastic mass which rose out of the pelvis about halfway to the umbilicus. A cystocele of moderate degree and a small rectocele were present. The cervix was posterior and normal except for small scar on the posterior lip. A cystic mass arose from the left adnexa and passed in front of the uterus. It was continuous with the mass felt abdominally. Blood pressure 150/72. Urine examination negative.

On March 11, 1934, following a curettage, a laparotomy was performed and a left ovarian tumor measuring 14 by 11 cm. was removed together with the tube. The right ovary was extremely atrophic. The uterus lay behind the tumor and appeared only slightly smaller than the organ of a female in active sexual life. Nothing further was done and the abdomen was closed. Convalescence was uneventful, the patient being discharged on the seventeenth day.

A hormone study was made by Dr. Raphael Kurzrok on the urine collected during the first twenty-four hours after operation. At least 8 rat units of female sex hormone per liter were found.

Pathologic Examination.—Ovary irregular, soft, cystic, mass 14 by 11 by 6 cm., greenish purple color, and made up of several loculi. On one surface was a small cystic area, contents of which have been evacuated; it apparently measured about 3 cm. in diameter. On section tumor was made up of numerous small cystic areas, the largest being approximately 4 cm. in diameter. The lining of these cystic areas was smooth, and they contained thin bloody fluid. Major portion of tumor, however, was formed by soft friable solid tissue which in turn had numerous minute cysts scattered throughout.

gether with the appearance of the endometrium show that in this particular case radium had no effect other than to mask the clinical picture by temporarily controlling the uterine bleeding. That this form of therapy did not affect the functional activity of this tumor, even for a short period, is suggested by the fact that menopausal symptoms appeared for the first time after the complete surgical removal.

While one is not justified in making assumptions on the basis of one case, nevertheless the following conclusions are suggested:

1. Radium, while very destructive to the normal follicular system in large doses, does not have the same effect on neoplastic granulosa cells.
2. Bleeding, accompanied by benign endometrial hyperplasia, in the postmenopausal woman, strongly suggests the presence of granulosa cell tumor. A laparotomy is justified in the presence of these findings.
3. The treatment of this type of tumor is surgical, unless there are strong contraindications to operation.

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PLACENTA ACCRETA FOUND AT CESAREAN SECTION

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FORTUNATE indeed is the one who finds placenta accreta at cesarean section rather than following vaginal delivery of the baby. Phaneuf¹ in 1933 collected 82 cases of placenta accreta and stated that the mortality rate was 72.1 per cent in cases where manual extraction of the placenta was done through the vagina; 5.8 per cent following delivery by vagina in cases where the diagnosis was made sufficiently early and in which abdominal hysterectomy was done; and 36.3 per cent in those cases of a similar class in which vaginal hysterectomy was done. From this follows the fact that the earlier abdominal hysterectomy is done after the discovery of the placenta accreta, the lower the mortality rate will be. I have been able to find in the literature eight cases of placenta accreta which were found during cesarean section (Table I). In all these cases, except one, immediate supravaginal amputation of the fundus was done with the result that all mothers and all babies lived. The following description of my case helps to substantiate the belief that practically all cases of placenta accreta are associated with other anomalies, the most common of which are the results of injuries to the endometrium by medication or instrumentation, fibroids of the uterus, diseases of the endometrium, placenta previa, or anatomic anomalies of the uterine body. As will be seen in a study of this case, there was a peculiar combination of abnormal circumstances.

CASE REPORT

A forty-three-year-old primipara was first seen by me June 6, 1925. Her history was negative except for a right oophorectomy four years before. Her last menstrual period was on Dec. 22, 1924. Physical examination at the time she consulted me revealed a six months' pregnancy with no abnormalities demonstrable, except a cyst of the cervix and a moderate anemia. At the end of her eighth month, Aug. 28, 1925, examination with a speculum revealed that the cyst on the cervix had increased considerably in size. It was as large as a lemon and over its posterior

position that the tumor was present at this time rests on fairly good grounds, inasmuch as the patient was bleeding from a hyperplastic endometrium at the age of sixty-five. The dosage of 3,000 mg. hours which was used is sufficient to completely destroy the follicular system in a young woman. However, while uterine bleeding



Fig. 2.—Low power microphotograph showing typical arrangement of granulosa cell tumor with folliculoid spaces.



Fig. 3.—High power microphotograph of same field.

ceased, the tumor continued to grow and was first noted clinically about one year later. About twenty-one months after the use of radium, the tumor was large enough to be apparent on abdominal inspection and uterine bleeding had recurred. The histologic appearance of the tumor and the hormone findings in the urine to-

Herein is described the ninth case, a primipara, aged forty-three years, with the baby in breech presentation, a large cyst of the cervix almost filling the upper vaginal tract, and an almost complete stenosis of the cervical canal.

Because of these complications a cesarean section was done and the placenta accreta found.

TABLE I. PLACENTA ACCRETA FOUND AT CESAREAN SECTION

NO.	AUTHOR	FATE*		COMPLICATIONS	OPERATION
		M	C		
1	Kwartin and Adler ³	L	L	Previous section Threatened rupture Hourglass contraction Thin scar	Supracervical hysterectomy
2	Solomons ⁴	L	L	Asymmetry of face of fetus Former dead baby Abortion Premature rupture of membranes	Hysterectomy
3	Reeb ⁵	L	L	Former premature birth Curettage Hemorrhage Inversion of uterus Salpingitis Peritonitis	Subtotal hysterectomy
4	Neumann ⁶	L	L	Twin pregnancy (one fetus pyracous) Abortion one year later Placenta previa	Hysterectomy
5	Neumann ⁶	L	L	Abortions Placenta previa	Manual removal of placenta
6	Joachimovits ⁷	L	L	Osteomalacia Contracted pelvis Atony	Hysterectomy
7	Bakanow ⁸	L	L	Perforation of uterus Ruptured uterus (due to growth of placenta through uterine wall)	Supravaginal hysterectomy
8	Breuer ⁹	L	L	Placenta previa Previous adherent placenta Vaginal infection (thrush) Bicornate uterus	Hysterectomy

*Fate: M—mother; C—child; L—lived.

A supravaginal hysterectomy was performed followed by a blood transfusion. When the fundus of the uterus was removed, an opening in the cervical canal from the inside could not be located. Both the mother and the baby lived.

Examination of the mother some months after operation showed that the cyst of the cervix had disappeared entirely and that the cervix had assumed its normal configuration.

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surface extended a vein as large as a match. Neither with the speculum nor with my finger by manual examination could I find the external os or any sign of a cervical opening. Apparently this must have been a pinpoint opening. The breech was below. The blood pressure was 110/60. The urine examination showed a slight trace of albumin. The height of the fundus was 34 cm. The patient had considerable pain in her back and sides. Because of the cervical cyst with the large vein on its posterior surface, the apparent stenosis of the cervix, the breech presentation, and the fact that the patient was a primipara at forty-three years of age, I decided to do a cesarean section at term.

The patient was examined at weekly intervals. The blood pressure remained at approximately 120/80. The height of the fundus increased to 36 cm. The baby remained in breech presentation. The urine was consistently negative. The cyst of the cervix, however, seemed to be growing in proportion to the growth of the uterus, so that at the time of the operation it practically filled the entire upper vaginal tract.

Several days before the estimated date of confinement a classical cesarean section was started, and the abdomen was opened to the right of the umbilicus for a distance of 12 cm., one-half above and one-half below the umbilicus. The uterus was opened and a male child weighing 4,285 gm. was extracted. On attempting to remove the placenta it was found to be grown into the myometrium and attempts to wipe it loose with a towel were of no avail. At each effort masses of placental tissue were left attached to the uterus. As considerable blood was being lost during the procedure, a rapid supravaginal hysterectomy was performed. At this time an effort was made from above to find a cervical opening inside the uterus, but none was apparent.

The patient suffered severe shock during the operation, but following a blood transfusion she had a normal postoperative course. On the twelfth postoperative day, because of severe backache, a vaginal examination was made. It was found that the cervical cyst had shrunk to the size of an egg; and a small dimple, which was probably the external os, could be felt. In the beginning of the third week she developed a phlebitis in the left leg with a fever of 101° F. This subsided gradually, and she left the hospital after a stay of forty-seven days with her left leg slightly swollen. Eight months after the cesarean section, examination revealed that the cyst was practically gone and only a very small external os could be seen.

The pathologic report on the removed specimen was: *Gross Examination:* Fundus of the uterus with placenta attached has been removed. Parts of placenta are very firmly attached to the uterus. No lines of demarcation can be made out on gross examination. The placental substance has apparently grown directly into the uterine tissue. A number of fibrous infarcts are present about the borders of the placental substance and they also have a very close contact with the uterine wall. The placenta is apparently no larger than normal size. Cord attachment is about two inches from one border. Cut sections through the placental substance show it to be apparently normal. *Microscopic Examination:* Section through the placenta and uterine wall shows no distinct line of separation. The covering of the placental villi is continuous with the connective tissue stroma of the uterine musculature. Some of the chorionic villi are in the formation of islands which are entirely surrounded by uterine muscle. The condition is characteristic of that described by Polak and Phelan² as placenta accreta.

Diagnosis: Placenta accreta.

SUMMARY

A review of the literature (Table I) revealed that eight cases of placenta accreta had been found at cesarean section, and a study of these cases showed that varied complications preceded or accompanied each one.

lower extremities not disturbed. Reflexes: all deep reflexes in the lower extremities were hyperactive. There was a positive Babinsky and Oppenheim on the left and positive Chaddock on the right. Ankle clonus strongly suggestive on the right. The abdominal reflexes were absent. Pain perception above the level of the third dorsal segment distribution was felt more clearly and promptly.

Roentgen examination of the chest failed to reveal a tumor but did reveal a marked scoliosis of the lower cervical and upper dorsal region of the spine.

Clinical Impression of the Neurologist.—Pressure against the spinal cord at the level of about the fourth dorsal segment.

Because of the above findings and because sterilization was strongly advised, delivery through the abdominal route was elected and she was so delivered of a full-term, living child which was normal in every respect. After her recovery it was found that she could walk a little but that there was still considerable weakness of the lower extremities. Two weeks after her operation an exploratory operation of her chest was performed and a dense massive intrapleural tumor was found. There was definite evidence of pressure over the region of the fourth dorsal vertebra. The tumor was entirely immobile and biopsy was taken. She was discharged with no change in symptoms.

Pathology.—Sections from the biopsy showed a mass composed of interlacing hyaline fibers between which lay elongated and spindle cells. There were many normal nerves and large encapsulated areas in which the nerve cells were compressed by intermingling hyaline fibrillae presenting an almost solid and nodular growth. A portion of the pleura attached to the growth showed a mild lymphocytic infiltration. There was no histologic evidence of malignancy.

Examination of the patient eight months later revealed the skin lesions still present but having subsided roughly to the extent of 40 per cent. The patient had been bedridden for the last six months and neurologic signs were accentuated to a marked degree. There was complete paralysis of both lower extremities; all forms of sensation were absent. Muscle sense of the lower extremities showed no change. The Babinski sign was strongly positive on both sides. A beginning atrophy of the lower extremities was noted. The systems otherwise were entirely normal. The baby showed no pathologic signs whatsoever, had progressed normally in weight and gave the general picture of a normal, healthy infant.

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Digonnet, Chenebault and Rouchy: Two Cases of Puerperal Phlebitis Treated by Novocaine Injection of the Lumbar Sympathetics, Bull. Soc. d'obst. et de gynec. 25: 215, 1936.

The authors report two cases of phlegmasia alba dolens which occurred during the puerperium and which they treated therapeutically according to the technic of Leriche, namely, by the injection of novocaine into the lumbar sympathetic system. The authors describe their technic in detail. They observed an immediate beneficial effect. The patient experienced a noticeable increase in heat and a rapid subsidence of the pain. The course of the phlebitis was considerably shortened.

J. P. GREENHILL.

PREGNANCY COMPLICATING NEUROFIBROMATOSIS WITH ASSOCIATED INTRATHORACIC TUMOR

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ALTHOUGH there are comparatively few cases of pregnancy complicating neurofibromatosis reported in the literature, the entire subject has been so completely reviewed and presented in the recent articles by Sharpe and Young and Kushner, that, to do so again would be useless repetition, therefore it is wished only to add one more case report as an additional observation of this interesting phenomenon.

Kushner, Hirsch, Nishizaki, Sharpe and Young have reported cases of neurofibromatosis aggravated by pregnancy. Sutton reports a case which subsided after pregnancy. Others have reported cases in which there was no change following pregnancy as is true of the present case. Wise and Eller observed a case appearing at the time of childbirth. The consensus of findings seems to indicate that pregnancy may reveal otherwise latent neurofibromatosis, that it may definitely aggravate preexisting disease and that following pregnancy symptoms may subside only to reappear with a succeeding pregnancy. The offspring may or may not show manifestations of the disease.

H. C., colored, aged twenty-one, primigravida, was admitted to the University Hospital at term, complaining of progressive weakness of the lower extremities and inability to walk. Her family history was noncontributory and her past history was negative except for the skin lesions which are characteristic of the condition and which had been present since early childhood. One year ago her legs suddenly became weak and the weakness progressed until she found she could not walk. She was seen in another hospital where a diagnosis of mediastinal tumor was made and exploratory operation advised. A large imbedded tumor was found pressing upon the upper dorsal and lower cervical vertebrae, biopsy diagnosis was that of neurofibromatosis (von Recklinghausen's disease). Despite the fact that no attempt was made to remove or change the position of the tumor, the original symptoms almost entirely disappeared, and she was fairly comfortable until about the thirty-sixth week of gestation when the symptoms reappeared and she was admitted to this hospital for study. Her past history prior to the original attack had been negative except for the skin lesions as noted above.

On admission, physical examination revealed a well-developed young colored woman whose whole body surface was covered with numerous macular, dark brown, pigmented areas which stood out prominently on her brown skin; they varied from 1 to 2 cm. in diameter. The lesions were not tender or painful and were circumscribed by an area of pigmentation lighter in hue although still darker than the surrounding skin. There was some limitation of expansion of the right chest and percussion note was slightly impaired at the base on this side. The abdomen contained a full-term pregnancy.

Neurologic Examination.—Muscle power, tone, and development of the upper extremities was in no way affected. All deep reflexes in the upper extremities were within normal limits. There was no disturbance of sensation. There was very marked weakness in both lower extremities. There was a slight hypertonicity of the lower extremities. Sensation: there was definite hypoesthesia to all forms of stimulation below the lower distribution of the third dorsal segment. Muscle sense of the

tion revealed a hand and arm down beside the head. Under ethylene anesthesia, the extremity was replaced and a large Voorhees' bag introduced. At 12:30 P.M., with the cervix fully dilated, the bag was expelled and the head descended to the pelvic floor. Delivery occurred spontaneously at 1:15 P.M. The third stage was normal with less than the usual blood loss, and the puerperium was afebrile.



Fig. 2.—Photograph with transillumination. The relationships are as in Fig. 1.



Fig. 3.—Roentgenogram. The relationships are as in Figs. 1 and 2.

The child, a normal male, weighed 3,650 gm. There was no asphyxia. The post-natal course was uneventful.

Routine examination of the secundines, which weighed 735 gm., revealed the conditions apparent in Fig. 1. In the membranes, a few centimeters from the edge of the mature placenta, two compressed fetuses of approximately the same size lay side by side, while beyond them was the compressed, atrophic placenta to which they were

TWIN PAPYRACEOUS FETUSES IN A TRIPLET PREGNANCY

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FETUS papyraceous (or compressus) is a well-recognized and not uncommon condition. In the usual case, one child of a twin pregnancy (usually binovular) dies from lack of nourishment at approximately the middle of the gestation period and becomes compressed between the amniotic sac of the surviving fetus and the uterine wall. Partial mummification ensues and at delivery the outlines of the fetus are visible in the membranes. Much more rarely, as in the following case report, a triplet pregnancy goes to full term with twin papyraceous fetuses and a single living child.

A. W., Hospital No. K4482, white, married, aged thirty-four years, was admitted to the University Hospital Sept. 20, 1934. Four previous single pregnancies had



Fig. 1.—Photograph by reflected light. The placenta of the normal child is on the left, with the papyraceous fetuses in the center, and the atrophied placenta of the twins in the retracted tissue on the right.

ended in the birth of normal children. In 1925, two partial thyroidectomies had been performed for cosmetic reasons, because of a large symptomless goiter. The last menstrual period began on Jan. 1, 1934, with the expected date of confinement Oct. 8, 1934. The pregnancy had been uneventful except for moderate nausea during the first trimester, and there had been no reason to suspect multiple pregnancy.

Examination revealed an apparently normal uterine pregnancy practically at term. Pelvic measurements were normal. There was a large adenomatous goiter associated with slight tachycardia (pulse rate, 90 to 130 per minute) and a basal metabolic rate of plus 46 per cent. Laboratory findings, including the blood Wassermann, were negative.

Following medical induction of labor with castor oil, quinine, and pituitary extract, labor pains began at 7:00 A.M. Sept. 26, 1934. The fetus lay in L. O. A. and the head was fixed. At 8:10 A.M., the membranes were ruptured artificially to stimulate contractions. At 10:00 A.M., when the cervix was dilated to 5.0 cm., rectal examina-

the true promontory of the sacrum. Naturally in multiparous women one has less difficulty in obtaining the diagonal and true conjugate because of the relaxation of the pelvic structures.

In using my instrument, the first three measurements, diagonal conjugate, true conjugate, and thickness of the pelvic bone are obtained as follows:

The small piece of the instrument is placed upon the long section which is held with the curve upward so that the upright arm is nearest to the curve. (Fig. 2). After examining and ascertaining the position of the promontory with the two examining fingers, the instrument is inserted alongside of the fingers with the curve upward and the shoulder inward. The instrument is worked into place past the side of the cervix upward to the promontory, placing and holding the shoulder of the instrument in place with the fingers or fingernail of the middle finger in the depression behind the upper end of the shoulder of the instrument. The left hand adjusts the upright sliding section beneath the pubic bone and the diagonal conjugate measurement is read off on the long section in centimeters. Then the left hand elevates the upright arm within the vagina and against the pubic bone; with

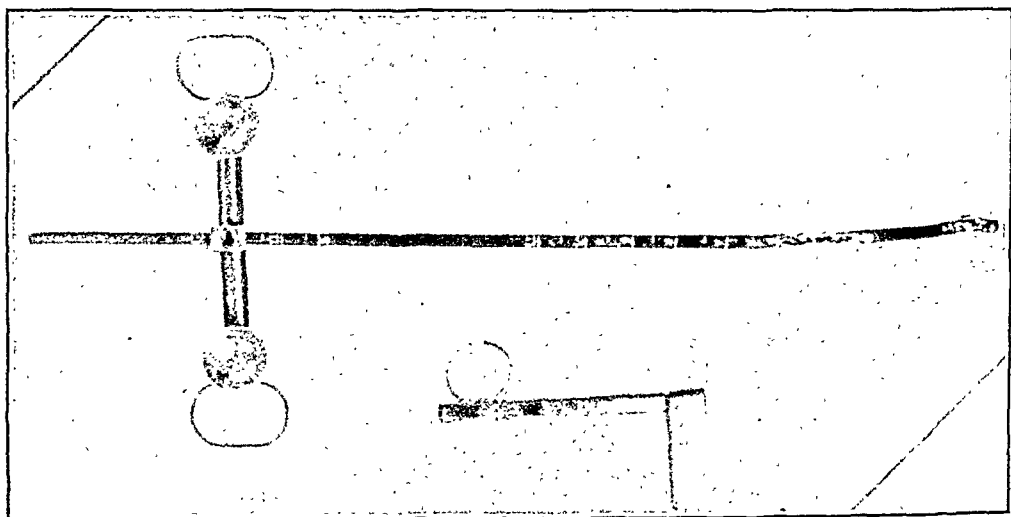


Fig. 1.—Internal and outlet pelvimeter. The long curved section has a transverse section slipped upon it for outlet measurements. The small section is slipped upon the long section after removal of transverse section and then used for internal measurements.

outward traction the true conjugate reading is seen upon the centimeter scale on the long section and the thickness of the pubic bone upon the small section scale.

Fig. 2 shows how this instrument is adapted to the pelvic inlet. These three measurements can then be taken whenever the examining fingers are able to distinguish the promontory of the sacrum.

These inside measurements should always be taken with caution, so as not to injure the cervix nor disturb the presenting part when it is in the pelvis. Naturally if the presenting part is below the brim, it is not necessary to measure the true or diagonal conjugate.

Continuing the use of these two pieces together, the anteroposterior diameter of the outlet can be obtained as also the depth of the pubic bone. This is done by placing the curved tip upon the end of the sacrum posteriorly while the upright arm is held just beneath the pubic arch, then the centimeter measure is read off on the shaft of the long member as you face it. This gives the anteroposterior diameter of the outlet. The depth of the pubic bone can be accurately measured upon the small section, anteriorly.

attached. A photograph, with a strong light source beneath the specimen, Fig. 2, showed the relationships more clearly, while the roentgenogram, Fig. 3, demonstrated the approximately equal development of the two compressed fetuses. The specimen was preserved intact and no attempt was made to determine by histologic examination of the membranes the essential character of the twin development, although it seems more probable that they were uniovular.

We are indebted to Mr. Frederick W. Kent, University Photographer, who took the photographs, and Mr. R. M. Tarrant who made the x-ray film.

AN INTERNAL AND OUTLET PELVIMETER, COMBINED

LESTER R. MELLOR, M.D., SYRACUSE, N. Y.

THE taking of the outlet as also the internal pelvic measurements in the past has usually been found very unsatisfactory. This fact has been observed quite generally by both obstetricians and general practitioners who have been doing maternity work.

These measurements which are so essential to the practice of good obstetrics have repeatedly been found wrong, due to various causes. First, the careless localizing of the anatomic points from which these measurements are taken. Second, the use of instruments which, although theoretically perfect, are practically of little value for everyday use.

Realizing the above difficulty and striving for better technic in this procedure, during the last few years, I have combined the best points of several instruments and, with essential changes, have developed the present combined instrument.

This instrument (Fig. 1) is made up of three parts: (1) a long curved four-sided section with the centimeter measure upon the front and back in the proper position for reading when in use, (2) a transverse, telescoping section fitted to slide upon the long piece, and (3) a short piece with an upright arm, which also slides on the long section, after removing the transverse member. The long section, with the transverse member fitted upon it, makes an outlet pelvimeter, while the small member replacing the transverse upon the long section becomes an instrument for internal pelvimetry.

The taking of the diagonal and true conjugate is usually a difficult and at times impossible undertaking, either with or without instruments, due to various reasons. First, in primiparas, the firm perinei interfere with the necessary upward pressure which the examining fingers must make to reach the promontory of the sacrum; second, the tilt of the pelvis makes it impossible to measure at times; third, a presenting part in the pelvis may make it impossible; fourth, some multiparous women have firm perinei which make the measurement difficult to take; fifth, pain, caused by the examination, may make it impossible without an anesthetic.

Naturally, if the promontory of the sacrum cannot be reached by the fingers of the examining hand, then one cannot hope to apply an instrument by hand to that point and be sure that it has reached its goal and, vice versa, if one can reach it with the tip of the examining finger, then it can be measured more accurately with an instrument.

I have repeatedly demonstrated the above observations to students, internes, and some fellow practitioners, also the possibility of confusing sacral ossifications with

This instrument is of special value in funnel and generally contracted pelves and in the accurate measurements of borderline cases, which naturally require the best judgment in their method of delivery.

Closer observation on these pelvic measurements and correct interpretation of their significance, when considering the best method of delivery to safeguard maternal and fetal life, cannot help but to improve our mortality and morbidity rate in the future.

Inasmuch as the biparietal diameter of the fetal skull is of such significance in borderline cases of pelvic contraction, I have been making biparietal notations in reference to fetal weight. In a small series of 100 cases, 93 per cent of babies weighing 6 pounds or over had a biparietal diameter of 9 cm. or more, while 84 per cent of babies under 6 pounds had a diameter averaging 8.4 cm. Only 3 babies under 6 pounds had a biparietal measurement of 9 cm. Generally speaking, bi-

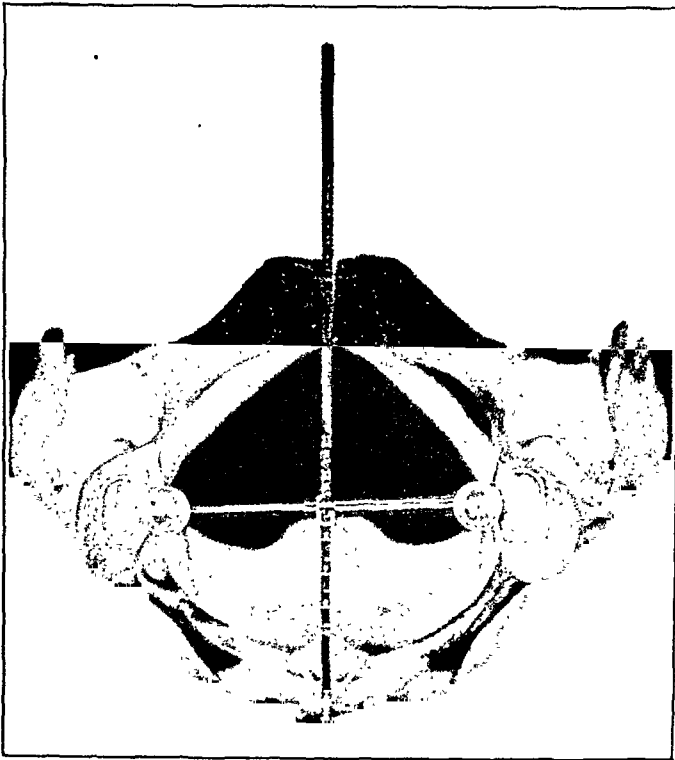


Fig. 3.—Outlet pelvimeter has been taped in place. Small internal section of instrument has been removed and transverse section threaded upon long section. Readings can be observed for both posterior sagittal and transverse outlet after instruments are removed as ratcheting keeps centimeter measure correct. Instrument made by Donald Thomas, 116 Windham Street, Syracuse, N. Y.

parietal measurements of babies at birth, weighing from 7 pounds up, did not increase with their difference of weight and were therefore usually as difficult to deliver at 7 pounds in contracted or borderline pelves as those weighing much more. Under 6 pounds, the biparietal diameter is usually markedly reduced from 1 to 1.5 cm., making delivery of these lighter weight children more successful in moderately contracted pelves.

Premature infants do not stand prolonged labor very well in contracted or funnel pelves and a closer check upon the fetal heart is advisable in these cases.

The saying that small babies have large heads and large babies relatively small heads must be considered the rule, unless you can prove otherwise in the individual case.

To continue the outlet measurements, remove the small member and put the transverse piece upon the long section as follows:

The transverse section is held with the centimeter reading to the right, while the long section is threaded into the window of the encircling band upon the crosspiece with the curve toward the patient and the shoulder end downward.

With the patient's hips well over the end of the table so that the sacrum is readily felt at its tip and free of pressure, you are now ready to measure the transverse of the outlet and the posterior sagittal diameter.

The instrument is held by placing the thumbs in the two oval rings, thumb nails facing each other and touching the measuring points on the instrument which are fitted to the tuberosities of the ischii. This measurement is made upon the tuberosities edge and not taken from within.



Fig. 2.—Showing use of internal pelvimeter, taking the true conjugate and thickness of pubic bone while in place. This demonstrates the curve in the long section so as to reach more fully the promontory when presenting parts, uterus or cervix, are in the way. Small ring under instrument is for traction to complete accuracy in measuring both the true conjugate and thickness of pubic bone on smaller instrument.

By proper palpation with the thumb tips going beyond and then returning, one eventually can most accurately secure this measurement, which becomes evident on the transverse bar as it is adapted to the perineum of the patient.

Next, by placing the thumb and first finger of the right hand into the cups on the transverse member and pressing firmly against the tissues to retain its position, the thumb and first finger of the left hand adjusts the curved section at its tip to the end of the sacrum, posteriorly. The posterior sagittal reading becomes evident at the lower inner edge of the window where the sections cross.

The instrument can then be removed, with readings unchanged, as the ratchets hold their adjustments (see Fig. 3). With this type of instrument, all measurement points are checked up with the finger tips and recordings are correspondingly accurate.

livery should be accomplished as quickly as possible in the interests of both mother and baby. The patient had already had 1/6 gr. of morphine and 1/150 of scopolamine five hours previously with rectal-ether-oil four hours previously.

Under deep ether anesthesia in the delivery room, it was found that the uterus was moderately tight but would relax and the presenting part could be displaced from the brim of the pelvis. Internal podalic version seemed to be the best method of delivery. The cervix was fully dilated and fully effaced. Because of the persistent tone of the uterus even under an anesthetic, 1/2 c.c. of adrenalin chloride 1-1000 was administered intramuscularly. Following this there was prompt relaxation of the uterine musculature, allowing internal podalic version to be accomplished with comparative ease. With the version completed a nine-and-three-quarter-pound male child was slowly extracted without difficulty. The after-coming head was delivered easily and without the use of forceps. The baby showed marked asphyxiation and pallor. Respirations were established artificially. The placenta separated spontaneously at the end of five minutes and was easily expressed from the vaginal vault and cervix without unusual bleeding.

After a change of gloves the birth canal was thoroughly explored. No lacerations could be detected in the vaginal vault, cervix, lower uterine segment, or fundus. The uterus seemed to lack tone and remained large, and there was a tendency to excess bleeding. This failed to respond to the usual oxytocics administered by hypodermic. The uterus and vagina were tightly packed with iodoform gauze. All bleeding was controlled. The fundus was now easily palpable as a firm ball rising two-thirds of the way to the umbilicus. The patient's general condition was good. The blood pressure was 130/90 and pulse 90. Patient was returned to bed.

About two and one-half hours after delivery the patient was suddenly seized with sharp pain in the right upper quadrant of the abdomen which radiated upward into the right shoulder. The pulse was 100 and the blood pressure 130/80. The entire abdomen was reported to be tender. Pain was controlled by morphine. Three hours later she again required morphine for the upper abdominal and shoulder pain. The patient was vomiting and was given 1,000 c.c. of normal saline, intravenously. I saw the patient at this time. Her general condition was good, and her abdomen was somewhat tender. The pulse remained at about 100 to 110 with no drop in blood pressure. There was no bleeding. Possible undetected uterine rupture was considered, but since the bleeding had been controlled and her general condition was good, laparotomy was not done.

During the night she required several hypodermics of morphine to control pain and restlessness. The pulse increased in rate up to 150 and temperature rose to 101°. There was profuse sweating. A blood count taken early the next morning about ten hours after delivery showed hemoglobin of 66 per cent, red cells 3,150,000, white cells 17,800 and polymorphonuclears 92 per cent. The white count repeated four hours later, that is, about fourteen hours after delivery, showed white cells 28,000 and polymorphonuclears 92 per cent.

Twenty-four hours after delivery her blood pressure was 120/90. There was generalized abdominal tenderness and distention, pulse was 140 to 160, and the patient was extremely ill. She was given a clysis of 5 per cent glucose, and arrangements were made for transfusion. Four hours later after receiving the transfusion the pulse was 152, the abdomen was more distended and markedly tender, and there was persistent vomiting. The blood count at this time was, hemoglobin 95 per cent, red cells 4,650,000, white cells 23,400, and polymorphonuclears 92 per cent. At this time it was our opinion that this patient was suffering from acute peritonitis probably due to a tear through the broad ligaments or through the uterus. Her condition was very poor. We felt that our only hope would be an exploration under local anesthesia.

Accuracy in pelvic mensuration becomes most important when the type of pelvis deviates from normal and the question of how to deliver to secure the best results for mother and child frequently presents a very difficult problem.

In my hands, this new pelvimeter has proved very useful, it is small, easily carried, easily read and surprisingly accurate when the anatomic points are first checked by the examining fingers.

608 EAST GENESEE STREET

RUPTURED UTERUS: PERITONITIS, OPERATION AND RECOVERY

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(From the Obstetric Service of the Knickerbocker Hospital)

AT THE Woman's Hospital, in the last thirteen years, there have been twelve cases of uterine rupture associated with pregnancy or labor. Eleven of these patients had prompt laparotomy with hysterectomy or repair. All these patients recovered. One patient was treated by tamponade together with transfusion. No laparotomy was done. This patient died forty-eight hours later of peritonitis and shock.

The case which I wish to present illustrates the difficulty in making a diagnosis of uterine rupture postpartum when the lesion is of minor degree. It also illustrates the dangers to which these women are subjected if the diagnosis and treatment are delayed.

Mrs. M. H., aged thirty-one years, white, gravida iii. She had had two previous spontaneous deliveries of normal babies at term.

She was admitted to the Knickerbocker Hospital Obstetrical Service Oct. 9, 1935, in the first stage of labor, at full term. Her antepartum period had been entirely normal. Her labor in the Hospital appeared to be uneventful for about eighteen hours, contractions occurring at three- to eight-minute intervals and of moderate severity. Examination on admission indicated a vertex presentation in right occipitoposterior position with the presenting part floating and gradually settling in and fixing in the brim. Sixteen hours after admission to the hospital and about twenty-two hours after onset of labor the membranes ruptured spontaneously. She was examined by the interne at this time, who found the presenting part wedged in the brim in what he considered to be right occipitoposterior position with the cervix fully dilated. The patient continued to have strong uterine contractions for the next two hours but as there seemed to be no progress in the descent of the child, he called an attending obstetrician.

I saw the patient shortly after this, probably from two to two and one-half hours after the rupture of the membranes and the attainment of full dilatation. It was evident that there was some obstruction to delivery. Contractions of the uterus were violent and prolonged. The fetal heart was irregular, carying from 100 to 160, with considerable passage of meconium. The patient's pulse was then 112 and temperature 101°. Vaginal examination revealed a face presentation with the chin to the left and posterior. This was wedged tightly into the brim of the pelvis, and there was no advance with the uterine contractions. While the baby was large, the patient had an entirely adequate bony pelvis and, due to previous childbirth injuries, there was no obstruction from the soft parts. It was apparent that de-

ABLATIO PLACENTAE TREATED BY CESAREAN SECTION, FOLLOWED BY HYSTERECTOMY

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CESAREAN section is considered by most obstetricians the procedure of choice as the treatment for ablatio placentae. In some cases this operation must be supplemented by the removal of the uterus. Where this is done at the time of the section, because of the hemorrhagic infiltration of the uterine musculature, the dangers are not especially great. Occasionally, however, at the time of the cesarean section, the surgeon feels that the uterus is contracting satisfactorily and yet the sequellae promptly show that this is not the case. Here it requires considerable judgment and courage to subject the patient to an immediate secondary operation to save her life. This is illustrated in the case referred to below.

Mrs. H. D., aged twenty-eight, para iii, gravida iv, had had three normal spontaneous deliveries; the previous medical and surgical history was negative. She registered in the Hospital in the eighth month of pregnancy and at the time of her two prenatal visits the following notations were charted: the blood pressure was 115/70; urine negative; Wassermann and Kahn tests negative; pulse 84; fetal heart present. She had a marked exophthalmos which she said had been present since the birth of her last baby. Her basal metabolism rate was plus three.

At eight A.M., March 22, 1935, when the patient was only eight months' pregnant, she was awakened by moderately severe abdominal cramps which she attributed to an intestinal upset. These pains became progressively worse and at twelve noon the patient had a severe vaginal hemorrhage and collapsed.

She was immediately transferred to the Hospital where external examination revealed a hard, tense, rigid abdomen, with a high fundus up to the ensiform. No fetal heart could be heard or fetal parts mapped out. The patient's pulse was imperceptible and the blood pressure was 70/50, and she was in profound shock. There was a steady flow of blood from the vagina. The patient was put in the Trendelenberg position, $\frac{1}{4}$ gr. of morphine sulphate was administered, and intravenous glucose and saline given. No vaginal or rectal examinations were made. One hour later, the patient recovered to some degree from the shock, the blood pressure had risen to 120/60, pulse 80 but very thin, and the vaginal bleeding, though diminished, was still present and continuous. The patient was typed and prepared for operation; the preoperative diagnosis was: separation of the placenta with concealed and revealed accidental bleeding.

Two hours after admission to the hospital a low classical Cesarean section was performed under general anesthesia. The uterus was blue and spotted with hemorrhagic areas, and when incised, revealed the placenta in front and completely separated, while the uterine cavity was filled with blood clots. The endometrium was irregular and shaggy.

The child, a male stillbirth, was delivered. Five millimeters of pituitrin was given intravenously and 1 c.c. of pituitrin injected directly into the uterine wall. The uterus was packed with iodoform gauze and then sutured in three layers. It contracted and remained firm and the normal color returned. The patient received a transfusion of 500 c.c. citrated blood during the operation.

Upon opening the abdomen it was found to be filled with dark serous blood-stained fluid, the peritoneum was dull and glazed as was the surface of the intestines in the lower portion of the abdomen. There was no fresh blood. The uterus was firmly contracted. I felt that there must be a uterine tear to account for the blood-stained fluid and slight iodoform odor as well as the peritonitis. However, no rent was at once apparent. A careful search revealed an area, far down on the right side posterior to the right broad ligament in the lower segment of the uterus, with a small hole about 0.5 c.c. in diameter into which a knuckle of iodoform gauze protruded. Only a minute opening was present through the peritoneal surface. The fluid was quickly evacuated from the abdomen with suction, and due to the extreme condition of the patient, the operation was rapidly terminated by placing three cigaret drains, the first at the site of the small hole in the uterus, second into the right flank and the third posterior to the uterus and into the culdesac. These were all brought out through the abdominal wound, since we did not wish to disturb the uterine and vaginal packing by bringing the drains through the vaginal vault. We believed that, if necessary, at a later date such dependent drainage could be established. The abdomen was closed with through-and-through sutures. She was given a clysis following this operation and this was repeated several times in the next few days. The stomach was drained by means of a Wangensteen tube for two days, following which she was able to retain food. The bowels responded to enemas, and the uterine gauze was removed twenty-four hours after operation.

The patient had rather a stormy convalescence for the first ten days after which the functions were normal, the temperature normal, and she was discharged from the hospital on the thirtieth day after operation with the wound nearly healed. Pelvic examination at that time was entirely negative.

COMMENTS

I believe that this woman must bear a charmed life and that we were very fortunate in the outcome of this case. Perhaps the selection of the method of delivery was unwise. Latzko extraperitoneal cesarean section might have been chosen. The rent in the lower uterine segment was so small that it was not detected when careful examination of the birth canal was made following delivery. The sudden abdominal pain radiating to the right shoulder together with the restlessness of the patient, the high leucocyte count with high rate of polynuclear cells, even without the signs of extensive intraperitoneal hemorrhage, should have been interpreted as due to uterine rupture, and laparotomy should have been done a few hours after delivery, rather than twenty-four hours later, when a well-developed peritonitis forced the issue. Certainly the risk to the mother would have been less.

59 EAST FIFTY-FOURTH STREET

Salberg and Brunet: *Trichomonas Vaginal Infestation: A Discussion of the Disease and Treatments*, Virginia M. Monthly 63: 223, 1936.

The authors state that they have tried and found unsatisfactory the following methods of treatment: (1) tincture of green soap, drying, and kaolin; (2) pyroligneous acid, boroglycerin; (3) stovarsol as a local application; and (4) silver picrate. At the present time they are using a powder consisting of oxyquiline, boric acid and talc after a thorough but gentle cleansing of the vagina, and feel that so far it has proved most satisfactory.

EUGENE S. AUER.

was observed in the clinic gave rise to a diagnosis of possible hyperthyroidism, but her pulse was only 84 and her basal metabolism rate was only plus-three. The peripheral neuritis of the right lower extremity may have been due to an impaired peripheral circulation, possibly the result of bandaging the extremities and thus shutting off the blood supply.

1882 GRAND CONCOURSE

PREGNANCY IN A PATIENT SUFFERING WITH SCLERODERMA

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(From the Service of the Margaret Williamson Hospital, Shanghai, China)

THE patient, a Chinese woman, aged thirty-one years, was admitted to the hospital on Jan. 30, 1933, at the end of her first pregnancy. She had been in labor for nearly forty-eight hours, and her membranes had ruptured twenty-four hours before admission. She had been treated by a midwife, who had torn or cut the perineum and vagina in several places.

General physical examination at the time of admission revealed a patient with a curious masklike facial expression. She had a more or less generally distributed edema, more severe over legs, thighs, lower abdomen, and vulva. The consistency of the edematous areas was much firmer than that of the ordinary edema of toxemia. Her knee joints were stiff, her legs fixed in extension, and her elbows were also stiff, with forearms fixed at about midflexion on the arms. The wrist joints were ankylosed, as were her hands, with fingers slightly flexed on the palm. Muscular wasting seemed limited in the main to the forearms. Her pulse was 110, her temperature normal, and her blood pressure 150/110.

Laboratory findings were as follows: Urine contained heavy albumin, and many granular casts. Blood examination showed hemoglobin 65 per cent; erythrocytes 3,500,000; and leucocytes 16,600, with 89 per cent polymorphonuclears.

Obstetric examination gave negative findings in pelvimetry, except that the Baudeloque was a little short, 18 cm. The abdomen was enlarged to the size of a full-term pregnancy, with the abdominal wall so firm as to preclude accurate palpation. Just above the symphysis, there was some pitting edema, but the fundus area of the uterus was almost boardlike in consistency. The sensation was much the same as that of her legs, thighs, and face. No relaxation of the uterus could be made out, and no fetal heart sounds were found. Rectal examination was unsatisfactory because of the edema of the vulva. Vaginal examination showed the cervix stiff, canal not wholly obliterated, and dilatation of 7 cm. Foul, meconium-stained amniotic fluid was escaping, and the fetal head was very high with the bi-parietal diameter above the inlet of the pelvis.

Differentiation or adjudication as to the relative influences of various factors was almost impossible. There was an obvious toxemia, with its edema; there might well be a tetanic uterus in view of the long labor; and there was the underlying scleroderma. The patient needed to be delivered and the most conservative available method seemed to be craniotomy. This had to be followed by embryotomy. The operation was very difficult, because the legs could not be bent on the thighs, and were held apart by nurses. In addition, the edema of both vulva and thighs made the outlet small and difficult of access. The child was a medium-sized female, and it is interesting to note that the extremities, particularly the lower, exhibited much

Following the operation the patient's condition was found to be poor; the pulse was imperceptible; the uterus not very hard, yet not high; there was continuous bleeding from the vagina, indicating that the uterine blood sinuses were still bleeding and unchecked by the uterine packing or pituitrin. A second transfusion of 350 c.c. of blood was given by the Soresi direct method one hour after the first, and one hour later, still a third transfusion was given of 500 c.c. of whole blood. Meanwhile, a packing of ten yards of iodoform gauze was tightly packed into the vagina and against the uterus, but within a short time bleeding again appeared at the vagina.

Consultation at this time decided that, although hysterectomy was the only procedure, the patient's condition was so critical as to preclude any further operation. Accordingly, the patient was left alone, supportive treatments being given meanwhile in the form of hypodermic stimulation, saline infusions, and bandaging of the extremities. At 8:35 that evening, six hours after the cesarean section, the patient was still alive but her condition was unchanged, pulse was imperceptible, blood pressure exceedingly low, and vaginal bleeding present and persistent. It was decided to operate again. Accordingly, under light gas and ether anesthesia the incision was reopened, the uterus delivered into the open wound and amputated supravaginally. At the same time, a transfusion of 600 c.c. of whole blood was started. The abdomen was closed with through-and-through silk sutures, the vaginal packing removed, and the patient put to bed. Clysis was maintained thereafter for the next twenty-four hours. Her condition remained critical for several days, but the pulse improved and there was no further bleeding.

During the next few weeks the patient steadily improved as to pulse, blood pressure, and general condition. Her temperature dropped from 102° to 100° on the third day and never went up beyond that during her entire stay in the hospital. The hemoglobin rose from 43 per cent on the third day after operative to 71 per cent shortly before discharge from the institution. The abdominal incision healed by primary intention and without any complications. About a week after the operation, the patient complained of soreness in the right lower abdomen and numbness and coldness of the entire right lower extremity. Shortly after there appeared a small area of superficial gangrene on the outer one-third of the right middle thigh and also on the heel. These necrotic areas became definite ulcers about the size of a quarter and were treated by means of cold quartz therapy, and cleared up in about two weeks. On April 24, a little more than one month after admission, the patient was discharged from the hospital and transferred to the clinic for baking and massage treatments to the right lower extremity.

This case presents the following interesting points: First, the patient survived two grave operations. At the time of the cesarean operation she was in shock and remained that way for at least eight or nine hours. Second, she was almost exsanguinated at the time of the second operation; although 1,350 c.c. of blood as well as 2,000 c.c. of saline were given, this flowed out of her vagina almost as rapidly as it was administered. So extreme was her condition that it was felt that the slightest operative procedure would precipitate a fatal issue. The cause for the continued bleeding is problematic; at no time either before or after the delivery were there any signs of toxemia or other predisposing causes for hemorrhage. There was nothing wrong with her blood pressure or urine at any time. Both Wassermann and Kahn tests were negative for syphilis. There was nothing apparent in the uterus either during the first or second operations, or in the gross or microscopic appearance that would account for the persistent bleeding. There were no signs of a fibroid or other pathologic condition in the uterine muscle. The uterus itself reacted very well to pituitrin; it remained fairly firm and contracted, but still the sinuses were open and kept bleeding. The exophthalmos which

BRENNER'S TUMOR

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(From the Pathological Department, Jersey City Medical Center)

THE unusually few cases of Brenner's tumor reported is due, in our belief, not only to an infrequency of occurrence but to a lesser extent, to the still esoteric features of the neoplasm. With this in mind we are reporting a case of solid cell Brenner's tumor.

Mrs. R. A., aged forty, was admitted to the Jersey City Medical Center, Aug. 28, 1935, complaining of a profuse vaginal bleeding of twelve days' duration. The family history was irrelevant. Her past history included a cholecystectomy three years before admission, and in the following year a right salpingo-oophorectomy and an appendectomy of which we were unable to obtain any information or record. She had been married twenty-one years and had three children, now living and well, who were delivered with normal parturition and postpartum courses. Menstruation began at the age of fourteen years, occurring every twenty-eight days and lasting three days. August 16, one week after a normal menstrual period, bleeding began and had continued until admission.

The general physical examination, with the exception of tenderness in the left lower quadrant, was essentially negative. Pelvic examination revealed a lacerated lobulated cervix with good pelvic support, a smooth elongated uterus freely movable and a small tender mass in the left fornix. The temperature was normal and the blood pressure was 112/80. The laboratory data noted a red blood cell count of 3,800,000 with a 70 per cent hemoglobin, Tallqvist, a white cell count of 8,200 with a differential count of 70 per cent polymorphonuclear leucocytes, 28 per cent lymphocytes, and 2 per cent large monocytes, eighteen minutes for sedimentation time, a negative Wassermann, and occasional red blood cells and a few epithelial cells in the urine.

On August 29, under spinal anesthesia, a supravaginal hysterectomy and a left salpingo-oophorectomy were performed. The right adnexa were not present. The right round ligament was firm and firmly attached to the anterior surface of the uterus which was enlarged, firm, and smooth. The left tube and ovary were densely adherent and fixed in the culdesac with numerous adhesions.

The postoperative course was uneventful and the patient was discharged Sept. 9, 1935. At the present time, she is well.

Pathologic examination revealed a uterus which measured 7 by 6 by 6 cm. The surfaces were smooth with the exception of the superior which was slightly roughened. On section, the wall attained a thickness of 1 cm. The endometrium was slightly raised and covered with a sanguineous material. The tube was roughened, thickened and adherent to the ovary. Microscopically, subacute endometritis, fibrosis of the uterus and chronic salpingitis were evident.

The ovary measured 3 by 2.3 by 1.8 cm. The peritoneal surfaces were smooth and lobulated with the exception of a roughened area which gave attachment to the tube. On section, the cut surfaces presented a roughly spheroidal, sharply defined, firm, grayish white nodular mass measuring 1.6 cm. in its largest diameter. This mass was eccentrically placed and at the hilum was surrounded by 0.1 cm. of ovarian stroma which gradually increased to attain the thickness of 0.6 cm. at the

the same subcutaneous woody sensation and adherence of skin to lower layers as that of the mother's body. Both of the child's feet were in the attitude of talipes varus, and the ankle joints were absolutely immobile.

The puerperium was comparatively uneventful, patient having fever as high as 101° daily until the fifth day, after which she was afebrile. Her blood pressure dropped rapidly, and by the fifth day was 112/60. Her urine was negative by that time, also. The edema disappeared, leaving the sclerodermic portions of her body unchanged. Her perineal and vaginal wounds healed badly, and she had very bad support on discharge.

One year and nine months later, the patient was again admitted, pregnant, at term, and in labor. She had had little if any midwife manipulation this time, and the fetus was alive in utero. Physical examination showed the same masklike facies, and the same condition of extremities as before. There was no evidence of superadded edema, and the abdomen was distinctly softer than on the first admission. Rhythmic contractions of the uterus were easily palpated. Blood pressure was 114/80, urine negative, and general condition good.

Delivery was by classical cesarean section. It was followed by supravaginal hysterectomy, because of the question of potential infection from manipulation before admission. The child, a female, was normal, and weighed 2,525 gm. The postoperative course was uneventful, with a slight elevation of temperature the first four days, without symptoms. The wound healed by first intention, and the patient went home on the twentieth day. A section of the abdominal wall taken at the time of operation is pathologically reported as showing "a definite increase in fibrous and connective tissue, subcutaneously."

The baby was on mixed feeding while in the hospital, and was discharged weighing 350 gm. more than at birth. She was breast fed at home, and was in good condition at eight months. She has since died of measles.

There is no history obtainable concerning the development of the condition, except that the patient herself says she has been as stiff as she now is since the age of eight. She believes the beginning of the stiffness dates from a fall which she had at that time. The sequence of events is almost certainly just the reverse, of course. The patient does not believe that there is any increase in the severity of the condition at present, and certainly there has been no appreciable change in the three years she has been under our observation.

There is such confusion among students as to the etiology and pathogenesis of scleroderma that no attempt is made here to discuss it. Multiple involvement or dysfunction of endocrine glands is the etiologic factor most often mentioned. Evidence of such dysfunction seems lacking in this patient. She has neither the mental sluggishness of a myxedematous individual, nor any of the nervous manifestations of Graves' disease. She is intelligent, active, and alert. Her menstrual history before marriage was negative, and she became pregnant two months after her marriage.

The case is reported mainly from the point of view of interest, and not because it is felt that the report in this form can make any scientific contribution to the subject of scleroderma in general.

nodules its arrangement closely resembles that of the interstitial lamellae as seen in compact bone. Surrounding the epithelial nests, the partially hyalinized fibrous tissue assumes a concentric arrangement to form narrow bands attaining a thickness of three or four cell layers. The epithelial nests are composed of groups of oval cells radiating to the periphery where they are limited by a single layer of fusiform or spindle-shaped epithelium parallel to the fibrous capsules. Their nuclei are oval or round, vesicular and dotted with a fine chromatin network. The cytoplasm is a delicately granular structure and only slightly acidophilic. The pericellular membranes are fairly well defined. Small round or oval vacuoles of the cytoplasm are often seen. The peripheral cells are conspicuous, for their smaller nuclei are comparatively rich in chromatin. The vascularity is poor. Mitotic figures are extremely infrequent.

CONCLUSIONS

1. The gross and microscopic findings are typical and the tumor is not to be confused with granulosa cell or epidermoid carcinoma.
2. The histogenesis is somewhat obscure but possibly related to the serous cystoma (Meyers).
3. The tumor is of a very low degree of malignancy, and once removed, the prognosis is usually good.
4. Better clinical and microscopic data should increase the number of cases on record.

I wish to thank Dr. J. M. Rector for allowing me to abstract the case and Dr. J. Goldstein for his valuable advice.

ACCIDENTAL RUPTURE AND SUCCESSFUL LIGATION OF AN UMBILICAL ARTERY BEFORE ONSET OF LABOR

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(From the Department of Obstetrics and Gynecology, University of Southern California, and the Los Angeles County Hospital).

MRS. C. B., aged thirty-five, entered the Los Angeles County Hospital at 1:30 p.m., Nov. 16, 1935, with the complaint of vaginal bleeding for five days.

The past history was not essential. She had had five full-term pregnancies, and two spontaneous abortions. The fifth pregnancy was complicated by polyhydramnion and stillbirth. Her largest baby weighed nine pounds and was delivered spontaneously.

The patient was due on November 13, and her pregnancy had been entirely uneventful until five days before admission, when she began to have slight vaginal bleeding, without pain. On the morning of entry, she passed two large clots, but at no time had the bleeding been excessive.

Physical examination revealed a moderately obese female appearing to be in good general condition, and showing no evidence of anemia. The findings were entirely negative except for slight pretibial edema and a blood pressure of 138/84. There were no uterine contractions and no vaginal bleeding on entry. All pelvic measurements were normal. The height of the fundus was 32 cm., fetus lying in L.O.A. position, fetal heart tones 148. Urine negative. Hemoglobin 70 per cent; R.B.C. 4,160,000; W.B.C. 11,000; 80 per cent polys. Wassermann negative.

In accordance with our usual procedures in cases of suspected placenta previa, no rectal examinations were done, but at 4 p.m. (after obtaining a suitable donor for

opposite pole. Within the ovarian stroma there were one lutein and several thin-walled cysts. Microscopic examination revealed an ovarian stroma supporting a

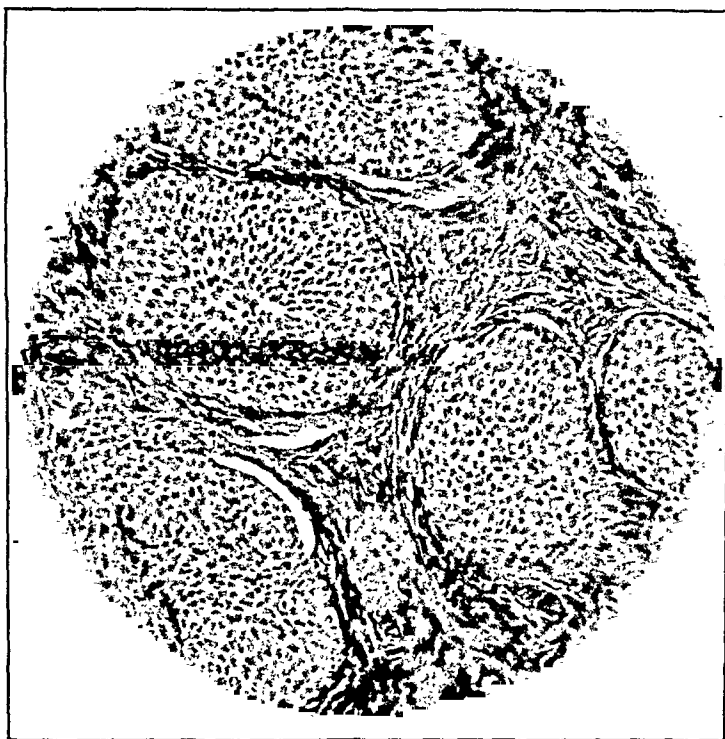


Fig. 1.—Low power magnification showing radiating groups of epithelial nests.

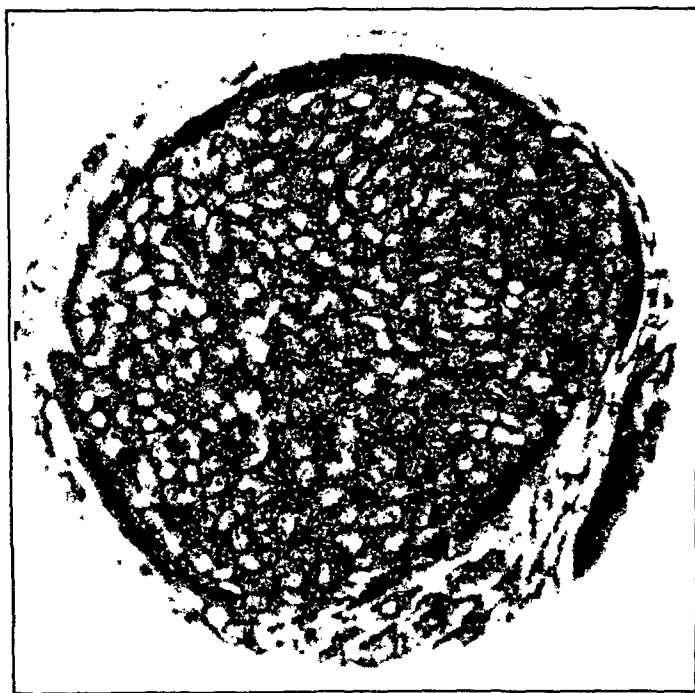


Fig. 2.—High power magnification of Fig. 1.

lutein and several follicular cysts. The tumor was well demarcated from the ovarian stroma by partially hyalinized, slightly acidophilic, elongated or oval-shaped cells, having a parallel arrangement. As the stroma dips down between the epithelial

maining artery, there is no deficiency in oxygenation of the fetal blood, since no asphyxia was noted in this case, and the fetal heart tones, once established after replacement of the cord, showed little variation in rate, rhythm, or quality. The case presented demonstrates the feasibility of ligating a bleeding vessel should such an accident occur.

Acknowledgment is made to Dr. E. M. Lazard and to Dr. Lyle G. McNeile for permission to report this case.

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HEMATOMETRA DUE TO ATRESIA OF THE CERVIX FOLLOWING CAUTERIZATION

A. L. HENKIN, M.D., BROOKLYN, N. Y.

CAUTERY treatment of chronic inflammatory lesions of the cervix is universally adopted at the present time; however, it is not without danger, and the purpose of this report is to call attention to this fact. The fact that great care must be used in the application of this modality was emphasized by others.

The case herewith reported is that of Mrs. J. A., aged twenty-two years, para i, grav. i, whose menstrual history was regular every month, moderate flow, and five days' duration with no pain. In April, 1936, she had a cauterization of the cervix for vaginal discharge and pain in the right lower abdomen. Following this treatment she did not menstruate in May and June; and because of pain and amenorrhea she was readmitted to the hospital where some operative procedure was performed, and she was kept in the hospital for three weeks. After her discharge she again failed to menstruate for two months. In August she was again admitted to the hospital for a dilatation of the cervix, which was followed by some bloody discharge. In spite of that she did not menstruate; so in October she was admitted to the hospital again for dilatation; but the patient was not relieved. At the expected time of her menstruation she complained of pain for three days, but there was no vaginal flow. On November 10 the patient was seen by me; her chief complaints were amenorrhea and pain in lower abdomen. Except for secondary anemia her general condition was negative. The local condition disclosed a multiparous perineum, absence of vaginal portio of the cervix; uterus the size of a three months' pregnancy with a mass in the right fornix the size of an orange. Speculum examination disclosed again an absence of the cervix except for a small dimple in the vault, where a small pinkish area of columnar epithelium was left.

A diagnosis of hematometra and hematocolpos due to destruction of the vaginal portio of the cervix by cautery was made.

Operation.—A tenaculum was applied to the vault of the vagina where the cervix was supposed to be; an incision was made in the anterior vaginal vault extending from a point one inch below the meatus down to the tenaculum; the vaginal wall was dissected laterally; the bladder was identified and retracted upward exposing what was left of the cervix. An incision was made into the cervical tissue which was

transfusion, if needed) a sterile vaginal examination was made. The cervix was found to be 50 per cent effaced, 2 cm. dilated, and fetal head floating in L.O.A. position. Placental tissue was felt at the margin of the internal os, confirming the diagnosis of placenta previa marginalis.

About 30 to 40 c.c. of blood were lost during the examination, and it was decided to rupture the membranes. A long hemostat was introduced through the cervix, the membranes grasped, and the instrument withdrawn. Unfortunately, there was a forelying cord which had not been recognized by the examining finger, and the loop of cord was withdrawn in the grasp of the hemostat. At the point of injury to the cord, dark blood spurted for a considerable distance with each pulsation. The bleeding point was ligated with a plain catgut suture and hemostasis secured. The cord was then replaced with some difficulty through the cervix, and a full dilatation (No. 5 Voorhees) bag was inserted and filled. Immediately after the insertion of the bag, the fetal heart tones became weak and irregular, rate 60; but by external manipulation, pressure was apparently removed, and the heart tones became regular, rate 150. The patient was returned to bed, and a two-pound weight was attached to the bag.

Active labor began at 7 P.M. (three hours after insertion of bag), and at 10 P.M., the cervix was 6 cm. dilated, 80 per cent effaced, with uterine contractions occurring every three minutes, moderate in intensity. Throughout labor, the fetal heart tones remained at the rate of 150. She was given $7\frac{1}{2}$ gr. of nembutal and $\frac{1}{150}$ gr. of scopolamine, and prepared for delivery. At 10:40 P.M., the bag slipped through the cervix, was deflated, and removed. Under complete anesthesia, a 6 pound 12 ounce male infant was delivered easily by version and extraction. The cervix and uterus were explored and found intact. The placenta was removed manually and the uterus packed with 8 yards of 8-ply gauze. Total measured blood loss was 350 c.c. The infant cried spontaneously and vigorously, showed no cyanosis, gained well, and left the hospital in good condition. Puerperium was normal, the highest temperature recorded was 99°, and the mother was discharged on November 27.

The umbilical cord measured 50 cm. in length and was attached centrally to the placenta. The latter appeared normal except for slight maceration at the periphery. One umbilical artery was ligated 30 cm. from the placenta. The umbilical arteries were probed and perfused with water. There was an apparent obstruction of one umbilical artery at the site of the ligature. This was confirmed by microscopic section taken through the suture, which was seen to pass around the artery. There was some effusion of blood into the substance of the cord, but otherwise it appeared histologically normal.

COMMENT

Complete rupture of an umbilical cord is fairly common, since over 700 cases are mentioned in the literature, whereas isolated rupture of one or more umbilical vessels is extremely rare. Forssell,¹ in 1908, classified the tearing of single cord vessels into three groups: (A) Rupture of a varix of the umbilical vein (eight case reports quoted); (B) rupture of a vessel with velamentous insertion (fairly common); and (C) the tearing of single cord vessels. In this last group, four writers have reported ruptures of the umbilical vein; Hamill,² Keller,³ Sackett,⁴ and Pahl.⁵ Injuries to one or both umbilical arteries have been reported by Wiere,⁶ Westphalen,⁷ Lonne,⁸ and Siddall.⁹ All of these last cases occurred during the delivery and were due to tearing injuries, two of the four accidents resulting in death of the fetus. In none of the cases reported was such an injury recognized prior to delivery, and there is apparently no recorded report of a living baby obtained following rupture of a cord vessel prior to labor, nor of an attempted ligation of a ruptured vessel.

It is interesting to speculate on the effect of occluding one umbilical artery in utero. Evidently, through arterial anastomoses or increased flow through the re-

The laboratory examination revealed nothing of note, the Wassermann and Kahn tests being negative, and the blood count and urinalysis within normal limits.

The patient was admitted to the Passavant Hospital and operation was carried out Apr. 8, 1935, under ether anesthesia. A bimanual examination revealed no abnormalities in the pelvis. The cervix was cauterized and then a solution of methylene blue was injected into the fistulous opening which immediately escaped from the anus. The right Bartholinian gland was exposed by an incision external to the labium minus, the dissection being carried out from the lateral aspect of the gland toward the duct. As the gland was being dissected and drawn out of its bed inward toward the duct, the upper limit of the fistulous tract became visible, some of the dye having stained the lateral inferior pole of the gland.

The entire fistulous tract was then laid open and completely dissected out, beginning at the lateral inferior aspect of the right Bartholinian gland going downward and outward to the external opening and then inward and backward to the pectinate line in the right upper quadrant of the rectum where the tract was amputated, leaving the internal fistulous opening.

Because of the extensive tissue removal extending from the vagina to the right ischiorectal space and rectum, it was thought advisable to leave the severance of the sphincter muscle until the wound had granulated in enough laterally and under the sphincter muscle to prevent retraction of the sphincter ends.

A double strand of black silk was guided into the internal opening of the fistula and tied about the sphincter muscle. The wound was packed with iodoform gauze, several loosely placed silkworm-gut sutures were inserted in the lateral margins of the wound, and the patient was returned to bed.

The packing was removed on the fourth day and the wound was loosely repacked. This procedure was repeated every third day, thus allowing the wound to granulate in from the bottom. On May 28, 1935, the wound had completely granulated in, there remaining only a small sinus, the bed of the silk ligature which formed a simple straight fistula. There was enough granulation tissue present about the sphincter muscle to prevent any retraction of the muscle ends should they now be severed and thus under direct infiltration anesthesia with 1 per cent novocaine solution, a grooved director was inserted into the internal opening, the tract laid open from above downward, the black silk "seton" removed, and the tract gently curetted. The sphincter ends barely separated with this incision and the patient was discharged from the hospital at the end of forty-eight hours. On June 21, 1935, the sphincter control was perfect and the wound healed.

The pathologic diagnosis submitted by Dr. R. C. Hamilton, Pathologist to the Passavant Hospital, was as follows: Ischiorectal fistula (tuberculous); miliary tuberculosis of Bartholin's gland; chronic Bartholinitis.

With the diagnosis of tuberculosis of both the Bartholinian gland and the anal fistula revealed, a roentgenogram was taken of the patient's chest on June 20, 1935, but showed no evidence of a tuberculous process, either old or recent.

445 UNION TRUST BUILDING

Williams, E. Ulysses: Ante-Natal Diagnosis of Quadruplets, *Brit. M. J.* 2: 1206, 1935.

The diagnosis of twins or triplets by x-ray after the sixth month of pregnancy is common, that of quadruplets less so. The author presents a case of quadruplets diagnosed at thirty weeks, and report is accompanied by plate. In the literature only one other instance of such diagnosis is found, that in Manchester in 1934.

F. L. ADAMS AND S. A. PEARL.

followed by a gush of black, thick tarry material. The finger was inserted into the cavity which had a closed pouch at the lower end which was bulging toward the rectum; while the upper end was surrounded by a ring of almost cartilaginous tissue which did not admit the tip of the little finger and from which the tarry material continued to escape; the vaginal mucous membrane of each side were then sutured with chromic sutures to the cervical mucous membrane on the corresponding side, thus forming a canal about an inch long which was open anteriorly. The patient had an uneventful recovery. Examination four months later disclosed a normal-sized uterus with patent canal which allowed free passage of a uterine sound.

The experience gained from the report of this case and to be emphasized is:

1. Whenever cautery is used in the treatment of chronic cervical diseases, the patient is to be kept under observation to prevent stenosis or complete atresia,
2. The indiscriminate use of cautery in the treatment of the cervix is not without danger.

It seems to me also that no cautery should be used in the presence of acute inflammatory lesions. A case of death following cautery of the cervix for endocervicitis in presence of acute infection is known to the author, but because of incomplete facts in the history it cannot be reported at present.

707 WILLOUGHBY AVENUE

TUBERCULOSIS OF THE BARTHOLINIAN GLAND

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TUBERCULOSIS of the bartholinian gland is a rare infection as shown by the scant reports of this pathologic entity in the literature. I am reporting a case complicated by an anal fistula also tuberculous and cured by excision of the bartholinian gland and fistula by a two-stage surgical procedure.

CASE REPORT

Miss L. B., a white woman aged thirty-two years, was seen March 28, 1935, with a history of having developed a painful swelling on the right side of her vagina four and one-half years ago. The gland was incised, drained, and two years later the swelling returned, necessitating a second incision and drainage by her family physician. An opening persisted on the right side midway between her vagina and rectum and has been discharging continuously since the last operation.

Her past history revealed a boil on the right side of her rectum eight and one-half years ago which was incised and continued to drain for four months before complete healing took place.

Four years ago she suffered a "nervous breakdown."

The general physical examination was essentially negative. The examination of the external genitalia revealed a hard, firm right bartholinian gland the size of a hazelnut from whose duct no discharge could be expressed. In the right ischio-rectal space about 2 cm. to the right and slightly above the anus was a fistulous opening, the size of a match head, from which could be expressed, both on pressure over the right bartholinian gland and on the perineum, a thick mucoid discharge. Probing of the sinus revealed extension upward but not into the right bartholinian gland and downward and backward toward the rectum above the anal sphincter.

Vaginal examination revealed a nulliparous cervix with an erosion the size of a dime. Bimanual examination was negative. A diagnosis of chronic bartholinitis, cervical erosion, and anal fistula was made and operation was advised.

12 were discharged with clinical cure and absence of bacteriologic evidence of gonococcal infection. After using a 25 per cent dilution of the filtrate once a week for a short time, it was thought wise to use a greater dilution more frequently, and the patients were given increasing doses of a 2.5 per cent solution of the filtrate twice a week. The table covers the principal facts. There were only two reactions; maximum temperature 101° F. and general malaise of about six hours' duration. One patient was discharged with persistent extracellular gram-negative diplococci, but apparent clinical cure.

These results are reported merely for purposes of comparison with those of other methods in the search for a satisfactory treatment of this condition. The approximately 70 per cent of good results is much better than that obtained previously in the Children's Clinic with local treatment.

164 MARKET STREET

EPIDEMIC PAROTITIS IN LATE PREGNANCY*

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(From the Department of Obstetrics and Gynecology, Harper Hospital)

JUDGING from the literature, mumps in the latter part of pregnancy is a very rare occurrence. When the complication was diagnosed in the case outlined below, consultation of several textbooks on obstetrics (Williams, DeLee, and Curtis) yielded no information whatsoever as to the prognosis or treatment. Only two relevant case reports were found in a rather thorough search through the periodic literature of the last twenty years. In 1931 Moore¹ described a severe manifestation of the disease about two months before term in the second pregnancy of a woman who already had a serious cardiac condition. The patient recovered after a hazardous illness but was delivered a month later of a stillborn macerated fetus. Recently, Dutta² of India reported the death of a primigravida at the eighth month who became affected during an epidemic of mumps among the native troops. She developed acute glomerular nephritis on the fifth day, was delivered of a stillborn fetus on the eighth, and died of the nephritis on the eleventh day. In addition to these two instances there was occasional mention of other cases, including one with transmission of the disease to the fetus in utero (Greenhill³), but no definite case reports or references were found. Two of Sinnecker's⁴ cases were possibly instances of epidemic parotitis occurring postpartum.

Mrs. J. A. D., thirty-one years old, primigravida. The last menstrual period occurred on July 25, 1935 from which the expected date of confinement was estimated for May 1, 1936. There was the history of pneumonia at nine years. Two years later (1917) she had had a tonsillectomy, adenoidectomy, and submucous resection of the nasal septum. Appendectomy was performed in 1922. In 1929 there had been a suspicion of pulmonary tuberculosis, but roentgen ray examinations at that time and again in January, 1935 were negative. In 1933 the patient had a severe attack of scarlet fever which, however, left no permanent kidney involvement. The general physical and obstetric examination showed nothing noteworthy, except some suppression of the breath sounds over the lower right side of the chest posteriorly, which was thought to be due to thickened pleura from pneumonia.

Except for moderate nausea and vomiting in the early months, the pregnancy was essentially uneventful until three weeks before the expected date of delivery. She was seen on April 9, 1936 because of swelling on the right side of the neck and

*Presented before the Detroit Obstetrical and Gynecological Society, December 1, 1936.

THE TREATMENT OF GONORRHEAL VAGINITIS WITH GONOCOCCUS FILTRATE

A. J. WHITEHOUSE, M.D., LEXINGTON, KY.

A MULTIPLICITY of methods and results reported for the treatment of any condition is usually indicative of the inadequacy of the procedure in use at the time. Consequent to a discussion of the unsatisfactory results of local treatment in cases of gonorrheal vaginitis in the Children's Clinic, the matter was taken up in the Gynecological Section of the Venereal Disease Clinic.

The lack of uniformity of results and the disadvantages of the use of the ovarian follicular hormone led to the search for some other more constant method and one amenable to the economic limitations and conditions of a Public Health Clinic. Many of the patients under treatment are children of mothers in the Venereal Clinic. Needless to say, the usual difficulties attendant upon a City Venereal Disease Clinic along lines of continuity of treatment and follow-up were encountered. Also, the premise on which the use of the ovarian follicular hormone has been based (the desquamation of an infected membrane) would seem not to comprehend the possible presence of some cervical glands, especially in those cases near puberty, and their infection by the gonococcus. Because bactericides do not reach the well-established infection hidden in the tissues, the production of immunity would seem to be the desired objective of research. However, the production of immunity to gonorrhea is more delicate and less stable than that to other infections. Corbus found that gonococcus filtrate or toxin prepared from a special medium, when injected intradermally, was capable of stimulating the body to the production of gonococcus antibodies. The willingness of the manufacturers of Corbus-Ferry gonococcus filtrate to furnish some of this material in the treatment of these cases led to its trial.

This report includes 30 children of whom: 5 patients refractory to the filtrate are receiving other treatment; 13 stopped before receiving adequate treatment; and

PATIENT	COLOR	SEX	AGE	25 PER CENT SOL.	DOSE	2.5 PER CENT SOL.	DOSE	LABORATORY	DISPOSITION
J. B.	C	F	12	c.c. 0.05		c.c. 0.05-1.0	(23 inj.)	Suspice.	Clinical cure
V. G.	W	F	10	0.05-0.55	(11)	0.05-0.55	(12 inj.)	Neg.	Discharged
B. H.	W	F	8	0.05-0.5	(10)	0.05-0.8	(13 inj.)	Neg.	Discharged
C. H.	W	F	6	0.05-0.5	(10)	0.05-0.8	(13 inj.)	Neg.	Discharged
B. J. H.	W	F	9			0.05-0.5	(9 inj.)	Neg.	Discharged
G. J.	W	F	7			0.05-0.3	(6 inj.)	Neg.	Discharged
V. J.	W	F	7	0.05-0.15	(3)	0.05-1.0	(22 inj.)	Neg.	Discharged
M. B. L.	W	F	9	0.05-0.7	(14)	0.05-1.0	(23 inj.)	Neg.	Discharged
M. L. M.	W	F	5	0.05-0.5	(11)	0.05-1.0	(8 inj.)	Neg.	Discharged
M. L. M.	C	F	6			0.05-0.4	(7 inj.)	Neg.	Discharged
A. M.	C	F	6			0.05-0.3	(6 inj.)	Neg.	Discharged
G. W. W.	W	F	7			0.05-0.3	(6 inj.)	Neg.	Discharged

5 cases being carried on.

13 stopped before adequate treatment.

PREGNANCY AND NEPHRECTOMY

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THE case herewith reported is that of a nephrectomy during the first month of gestation, the latter being undiagnosed, which was followed by a normal pregnancy, labor, and puerperium.

Mrs. A., a twenty-four-year-old white woman, first seen by me on March 15, 1935, at which time she complained of nausea of ten days' duration and pain in the right kidney area, which had been present at intervals since 1932. She thought she might be pregnant. The last normal menstrual period was March 4, 1935. Menses had always been regular and normal.

In 1932, she delivered a six and one-half months' macerated stillbirth, at which time she had pus in the urine and hypertension. This had never been treated. She had had no other pregnancies, and the rest of her history was essentially negative.

Physical examination was negative except for tenderness in the right costovertebral angle and large amounts of pus cells in the urine. Blood pressure was 110 systolic and 70 diastolic. I could find no evidence of pregnancy at this time.

She was referred to the Department of Urology at the Evanston Hospital for diagnosis and treatment. She entered the hospital March 28, 1935. A cystoscopic examination was made by Dr. James Farrell who made a diagnosis of right ureteral calculus and right pyonephrosis. The urine showed a 3-plus albumin, few red blood cells and many white blood cells.

Blood count showed 96 per cent hemoglobin; 5,400,000 red blood cells and 13,900 white blood cells. Blood chemistry was normal.

Phenolsulphonephthalein test revealed the following:

First specimen, 40 minutes after dye injection, 57 c.c. or 13.2%	
Second specimen, 70 minutes after dye injection, 46 c.c. or 14.2%	
Total	<u>27.4%</u>

On April 1, 1935, a right nephrectomy was done by Dr. Farrell. This was followed by a normal postoperative course and with discharge from the hospital on the fifteenth postoperative day.

I again saw this patient on May 17, 1935, at which time I found a two and one-half months' pregnancy. The pregnancy followed a normal course with normal urine and kidney function.

Labor began spontaneously at 6 P.M., Nov. 28, 1935. The patient received $7\frac{1}{2}$ gr. of pentobarbital and 1/150 gr. of scopolamine. At 10 P.M., four hours after the onset of labor, the membranes ruptured and following this one foot prolapsed. She was found to be dilated completely at this time. A left mediolateral episiotomy was done following which the breech and shoulders were delivered with manual aid. Piper forceps were used on the after-coming head. The placenta, which was normal, delivered spontaneously and the episiotomy wound was repaired under gas anesthesia. The baby weighing 5 pounds 6 ounces was perfectly normal.

The puerperium was normal. The blood chemistry, kidney function test, urine and blood pressure were all normal when the patient was discharged from the hospital on her eleventh postpartum day.

The mother and baby were both in excellent condition at the final postpartum examination, six weeks after delivery. The baby was fed entirely with the mother's breast milk.

face. This had been preceded by several days of general malaise. The temperature was 99.6° F. Behind the angle of the jaw on the right and pushing up the lobe of the ear was a soft, doughy swelling which extended upward in front of the ear and forward over the masseter muscle. There was also puffiness below the left ear. The throat was slightly injected, and the orifices of both Stenson's ducts were swollen and reddened. By the next day the swelling had greatly increased on both sides, giving a typical picture of epidemic parotitis. There was no history of exposure, though the patient stated definitely that she had never had mumps. Treatment consisted of bed rest and analgesics for pain and stiffness of the jaws. The patient, a graduate nurse, made frequent readings of her temperature which never went above 100° F. Swelling began to subside on the fifth day and had entirely disappeared by the twelfth.

On May 13, 1936, after a labor of twelve hours induced by castor oil and quinine, the patient was delivered spontaneously of a male child weighing seven and one-fourth pounds and appearing normal in every respect. The puerperium was afebrile and normal, and the child gained satisfactorily on breast feeding supplemented by evaporated milk formula.

This case is of interest for two reasons:

1. Because of the apparent rarity of epidemic parotitis complicating pregnancy. This is the only case to occur among the 5,000 to 6,000 private and clinic obstetric patients whose clinical course has been known to me. Greenhill³ stated that there had been only one such instance at the Chicago Lying-In Hospital in 35,000 deliveries.

2. Notwithstanding the prognosis obtained from the few reports in the literature, the disease ran a mild course and caused no difficulty. It seems possible that only severe cases have found their way into the literature and that there are many others of such slight gravity as to appear unworthy of comment.

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955 FISHER BUILDING

Dodds, Gladys H.: The Visscher-Bowman Test for Pregnancy, Brit. M. J. 2: 224, 1936.

Visscher and Bowman described the following chemical test for which they claim great accuracy: To 1 c.c. of urine are added one drop of 1 per cent hydrogen peroxide, five drops of a 1 per cent phenylhydrazine hydrochloride solution in water, five drops of a 5 per cent methyl cyanide solution in water and 5 drops of a concentrated hydrochloric acid. The mixture is heated in a water-bath for twenty-five minutes.

A russet color and thick flocculent precipitate denotes a strongly positive reaction; a dark brown and slightly flocculent precipitate shows a weakly positive result. A brown color and slight powdery precipitate shows a doubtful negative result, and no color change with no precipitate denotes a negative test.

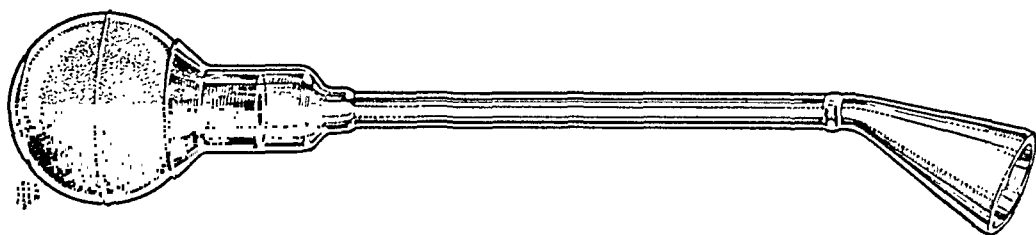
The author investigated 100 pregnant patients and obtained correct results in 90 per cent of cases. In nonpregnant women the test was correct in 88.8 per cent. The percentage of error among the nonpregnant group is too high to make the test of any real value.

F. L. ADAIR AND S. A. PEARL.

CERVICAL SUCTION SYRINGE

THOMAS L. ROGERS, M.D., LONG BEACH, CALIF.

AS THE cervix has been called the tonsil of the pelvis, the suggestion has been made that a Hurd tonsil suction syringe tube would prove a satisfactory device to remove tenacious mucous plugs from the cervical canal and ducts. This affords a method of obtaining material for smears for diagnosis and also as a cleansing measure preparatory to local applications. Having experimented with the Hurd tube, I found the angle too acute and also felt that if the opening were made circular and larger in diameter, the application would be more effective. At my



request the Becton, Dickinson Company has adapted their regular tonsil suction syringe by lengthening the straight tube and welding on at a 20 degree angle, a funnel-shaped tip with circular opening, either one inch or seven-eighths inch in diameter, inside measurement, as desired. This apparatus has the advantage that the bulb is interchangeable, low priced, and the only deteriorating element. The device can be readily manipulated with one hand and the tip always in sight, it provides adequate suction for the removal of mucopus and establishing drainage. An additional effect is the slight hyperemia produced, which may have a favorable influence on the inflammatory process.

703 PACIFIC AVENUE.

Schwartz, I.: Gruskin Intradermal Test for Pregnancy, *Am. J. Surg.* 33: 225, 1936.

The simplicity of the test, the rapidity with which diagnosis is made, and the high incidence of accuracy are striking. In the author's series, the test was correctly positive in 96 per cent of 155 pregnant women, and was correctly negative in 90 per cent of 66 nonpregnant women, and all male controls. A group of individuals with disturbed metabolism, usually of endocrine origin or with skin anomalies, are inherently incapable of determinable skin testing. Disregarding this very small group, the test permits of routine application and its validity is asserted by the high percentage of accuracy obtained.

J. THORNWELL WITHERSPOON.

VELAMENTOUS INSERTION OF THE UMBILICAL CORD

A. J. WHITEHOUSE, M.D., LEXINGTON, KY.

(From the Obstetrical Service of St. Joseph Hospital)

THE rarity of a condition imposes the necessity for careful study of every case. Insertio velamentosa is defined as the condition in which "the vessels of the umbilical cord separate at varying distances from the placenta and reach their placental termini by taking their course between the amnion and chorion, or are enveloped in a fold of the former tissue." The incidence is considered about 1 per cent, being higher in multiple than in single pregnancies. Moderate bleeding during the first stage of labor, in the absence of evidence of placenta previa or abruptio placentae, is mentioned as a sign of a condition naturally difficult to diagnose. This follows rupture of its vessels. Only by palpation within the cervix of the pulsating cord vessels over the bulging membranes is absolute diagnosis possible. The condition was not diagnosed antepartum in the case presented.

D. D., twenty-one years old, white, housewife, came under prenatal supervision Nov. 16, 1935. Her last menstrual period began Sept. 6, 1935; menses having been regular and normal previously. Her past history revealed no operations or serious illnesses, except typhoid fever at seven. On May 14, 1935, the patient, on being hospitalized for pyonephrosis with temperature of 104° F., had a spontaneous premature labor at seven months: the baby lived two hours. There were no other pregnancies. The family history was irrelevant.

The present pregnancy was uncomplicated. The patient had a normal increase in weight of about 21 pounds: her blood pressure had ranged from 94 to 110 systolic and 54 to 66 diastolic. There was no edema, no visual disturbance or headache, and no albuminuria. Her medication included 0.5 to 1 gr. of thyroid every day; an iron preparation, feosol; a fortified cod liver oil; and a course of "Urophosphate," after urine had shown some pus cells at seven months. She felt quickening on Dec. 7, 1935. On May 16, 1936, at 5 A.M., labor began spontaneously and fetal movements were felt. There was no bleeding. The presentation was right occiput anterior. She was given sodium amytal and morphine sulphate early for analgesia. At 11:15 A.M. (about six hours after onset of labor), under light drop ether anesthesia, the patient had an easy spontaneous delivery of a stillborn male fetus weighing 5 pounds 4 ounces. The baby was given an intracardiac injection of adrenalin with no response. It appeared to be a well-developed but marasmic full-term baby. An examination of the placenta and membranes revealed the insertion of the intact umbilical cord in the membranes about 3 cm. from the margin of the placenta. There was no evidence of blood vessel rupture. Autopsy revealed no other demonstrable cause of death.

The condition is reported as a possible etiologic factor in stillbirths not otherwise explained.

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Oviducts persist in the males and with high dosages become greatly swollen in both sexes. Wolffian ducts (incipient vasa deferentia) remain unmodified.

The asymmetrical differences so noticeable in the response of the two testes are attributed to a germinal epithelium (incipient ovarian cortex) which forms in early development only on the left testis.

With the synthetic male hormones, androsterone, dehydroandrosterone, androstenedione, in doses of from 0.02 mg. to 1 mg., the form and histologic structure of the right ovary of the genetic females are changed to that of a testislike organ. The ovarian medullary tissue is transformed into testis tissue. The left ovary becomes narrower and more rounded than normal and exhibits a thinning of the ovarian cortex and hypertrophy of the ovarian medulla and its inversion to testis tissue. The oviducts of the females undergo a regression beginning distally. Wolffian ducts (potential vasa deferentia) of both sexes are enormously swollen. Within the range of dosages noted above the male gonads remain more or less unaffected. Other workers (Wolff and Ginglinger) using larger dosages (0.5 to 2 mg.) have obtained estrogenic effects in the female, i.e., formation of ovarian cortex on the left testis and persistence of oviducts in male embryos. With male hormone preparations from human male urine, however, in the present experiments definite estrogenic effects were obtained, whether or not the preparation showed the presence of female hormone as detected by the vaginal smear test. In general, recent work with sex hormones in the chick embryo seems to show that it takes more male hormone to bring about reversal of the females than it takes female hormone to bring about reversal of the males.

As regards the manner of action of these hormones, it appears that the male hormones bring about a response of all the potential male components of the bisexual embryonic reproductive system while the female components respond only to the female hormones.

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Editorial Comment

Reversal of Sex in the Chick Embryo by the Action of Male and Female Sex Hormones

RECENT experiments by B. H. Willier of the Biological Laboratory of the University of Rochester in collaboration with F. C. Koch and T. F. Gallagher of the University of Chicago (*Physiological Zoology*, January, 1937) have shown that it is possible to alter the sex of chick embryos by injecting known quantities of male and female sex hormones into the developing hen's egg. The female hormones, theelin and theelol (crystalline form, dissolved in ethylene glycol), and the synthetic male hormones, androsterone, dehydroandrosterone, androstenedione (dissolved in propylene glycol), have been used, as well as male hormone preparations from human male urine and bull testis.

Briefly, the method consists of making a single injection of the solutions directly into the albumen through a minute opening in the shell, after forty-eight hours' incubation. Development is continued until just prior to hatching when the embryos are removed from the shell and examined carefully for any changes which may have occurred in their urogenital systems.

With theelin and theelol, dosages ranging from 0.05 mg. to 2 mg., the histologic structure and form of the left testis of the genetic males are markedly modified, consisting of a central core of medullary tissue upon which is superimposed a thick ovarian cortex. The right testis remains testicular in structure but is often smaller than normal. In extreme cases (1 to 2 mg.) no traces of testicular tissue remain in the left testis, reversal is complete, and the gonad is almost indistinguishable from a normal female ovary. In such cases the right testis usually becomes quite flat, reduced in size, and contains ovarian medullary cords. In the genetic females the gonads remain unaffected with the exception of an occasional increase in ovarian cortex on the right.

Laterally attached is the gluteus maximus and at the tip is the attachment of the anal sphincter. The lower strands of the sacrosciatic ligaments are attached near the cornua.

The nerve supply of the region is rich. On the dorsal surface, the posterior divisions of the lower three sacral nerves form loops and, with the coccygeal nerve, supply the skin over the lower end of the coccyx, and send filaments to the posterior coccygeal ligaments. The coccygeal plexiform arrangement of nerves, found along either side, is formed mainly from the anterior divisions of the fifth sacral and the coccygeal nerves. Upon the ventral surface of the coccyx the two symmetrical sympathetic trunks unite and terminate in the single median sympathetic ganglion-coccygeum impar. This ganglion connects with the branches of the fifth sacral and coccygeal nerves, thus forming an extensive plexus on the anterior coccygeal surface. Filaments from this plexiform arrangement pass to the tenomuscular insertions of the levator, coccygeus gluteus maximus muscles, and the sphincter ani. The plexus also innervates the sacrococcygeal joint and ligaments.

Thus it is apparent that the structures which enter into the fusion or support of the sacrococcygeal joint, or influence mobility of the coccyx on the sacrum, are richly supplied by filaments from the coccygeal plexus. Involvement of the sympathetic system through the ganglion impar elucidates to a certain extent the variety of symptoms and the varied causative factors which the condition of coccygodynia may engender.

TYPES OF COCCYGDYNIA

It necessarily follows from the above considerations that coccygodynia may be of different types. In this presentation these are arbitrarily grouped as follows:

1. Reflex coccygodynia
2. Traumatic coccygodynia
3. Neuralgia or neuritis of the coccygeal plexus.

Reflex Coccygodynia—Organic and Psychogenic.—Reflex coccygodynia is symptomatic of systemic disturbance removed from the local site. It is of two types, organic and psychogenic. Some of the conditions which may be listed under organic reflex coccygodynia are rectal tabes, meningiomas, spinal fractures, spina bifida occulta, and postmeningitic states. Personally, we have seen none of these, although they are mentioned by Simpson, Drueck, Kleckner and others. Many patients are seen with rectal troubles, especially fistulas, piles, proctitis, and fissures, where there is referred perianal pain erroneously referred to the coccyx. Only a careless examination could fail to reveal the true type and cause of pain. They do not cause coccygodynia, but coexistence with true coccygodynia may produce embarrassing confusion.

Psychogenic coccygodynia is attributed to hysteria, neurasthenia, psychoneurosis, traumatic neurosis, and patients with "irritable spine"; somewhat frequently seen as a causative factor is definite sex imbalance or maladjustment. Hamill recites an interesting case based upon hysteria and expresses the opinion that the spasmodic pains of coccygodynia are analogous to vaginismus, and that all cases should be handled by psychotherapy. Except for reflex coccygodynia of psychogenic origin, which is by no means common, this view is at variance with most clinical opinion and experience.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

A CONSIDERATION OF THE TYPES AND TREATMENT OF COCCYGODYNIA

EDWARD G. WATERS, M.D., PH.B., F.A.C.S., JERSEY CITY, N. J.

COCCYGODYNIA is a painful neuralgic condition of the tissues in the sacrococcygeoperineal region. It is relatively common in women under forty years of age, is highly disabling and painful, bizarre in its manifestations and types and involves an indeterminate pathology. It is given little attention in literature, texts, or from the profession, and less treatment. Sporadic contributions have discussed the subject matter, but their effects are not lasting. In general, they stress the form of treatment favored by the author, and treat all coccygodynias as a group. The valuable paper of Youngs was "lost" but that of Youmans aroused interest in nonoperative treatment of the condition. The more recent contributions of Lewin and Kleckner, who review the literature, stress the importance of selective therapy, but there still exists a tendency, in most papers, to regard the condition and its treatment as essentially surgical.

ANATOMIC FACTORS OF IMPORTANCE

Full understanding of the causes, symptoms, effects, and treatment of coccygodynia is dependent upon adequate appreciation of certain anatomic structures. The coccyx is the osseous fusion of the five terminal spinal vertebrae. It is joined to the sacrum above by ligamentous union, and follows its general curvilinear direction. Exceptionally it may be fused or ankylosed. The two coccygeal cornua extend upward from the posterior surface and form, through ligamentous connections with the sacral cornua, important foramina. These transmit the branches of the fifth sacral nerve, the importance of which will be presently seen. The coccyx in the female, in contrast to the male, fuses with the sacrum late in life, if at all. The sacrococcygeal articulation is a false synchondrosis with anterior, superficial and deep posterior, and two lateral ligaments, with a fibrocartilaginous disc interposed. These structures undergo physiologic alterations in late pregnancy which permit increased mobility during parturition. This is especially true of the fibrocartilaginous disc and the anterior ligament. It is highly probable that the relative exposure of the coccyx in female pelvic conformation is an important element in accounting for the greater incidence of coccygodynia in women.

The anterior coccygeal surface has attached to it the levator ani and coccygeus muscles and is in close relationship to the posterior rectal wall.

TREATMENT

The partition of coccygodynia according to causal type simplifies the problem of therapy. In reflex coccygodynia, no benefit may be expected from purely local therapy. A careful history and examination of the entire patient with detailed observation of the exact type, location and radiation of pain should reveal the cause for reflex coccygodynia. The proper and only effective treatment is to deal with the causative condition. It is well to remember that more than half of the reflex coccygodynias are caused by sexual imbalance or maladjustment. The physician interested in these peculiarly human problems can completely relieve the sufferer by combining psychotherapy with alleviation or correction of the sexual disaffection.

Treatment of traumatic coccygodynia is definite. In the acute stage, bed rest is indicated with local applications of heat in the form of hot sitz baths, hot oil rectal instillations, hot rectal douches, diathermy or short wave therapy. A dislocated coccyx is manually reduced, if possible. Analgesics and sedatives are certainly indicated, with dosage sufficient to give clinical relief. The acute phase is over in ten to twenty days, and the patient often obtains complete relief in spite of a persisting coccygeal deformity. When the pain becomes chronic, resort may be had to two lines of action, radical or conservative. The radical procedure of coccygeal excision, although surgically simple, should be deferred until conservative therapy has received a thorough trial. The coccyx serves as an important point of musculotendinous attachment, and its removal leaves some degree of pelvic weakness. The operation may be complicated by a disabling infection, and not infrequently after the coccyx is out, the pain still persists. Therefore the operation is neither to be suggested nor lightly undertaken until conservative measures fail, or unless there is gross deformity, caries, osteomyelitis or coccygeal periostitis with pericoccygitis.

Neuralgia and neuritis of the coccygeal plexus are best treated by direct attack on the plexus. Injections of novocaine, alcohol, benacol, quinine and urea hydrochloride, sodium morrhuate, and saline were used in this series. While all were found of some value, the most useful solutions were 2 per cent novocaine in 2 c.c. to 10 c.c. amounts, and $\frac{1}{2}$ to $1\frac{1}{2}$ c.c. of 80 per cent alcohol. From one to six injections of novocaine are required, and the relief obtained is usually permanent. Injection of alcohol, suggested by Youngs and Youmans, follows DeVesian's application in 1907 of trifacial nerve injections based upon Schlosser's principles. These are more definite and lasting in effect, but they are also more painful; two of our patients had prolonged pain with induration, redness, and swelling which lasted for ten days, following a 3 c.c. injection of 80 per cent alcohol. Rather marked induration and inflammatory edema may be expected in the perineal body and pericoccygeal tissues should more than $1\frac{1}{2}$ c.c. of 80 per cent alcohol be injected. This tender area gives rise to an aching sensation in the rectal region for a week or more, but it is generally tolerated better than the coccygeal pain which it supplants. Some degree of asymptomatic tissue induration is commonly seen even with small doses.

The following is a description of the technic employed in our cases. The patient is placed in the right lateral Sims position for all injections, excepting those made on the anterior surface or concavity of the coccyx, when the exaggerated lithotomy position is used. The gloved index

Traumatic Coccygodynia.—Coccygodynia of traumatic origin is the oldest of recognized types. There may be an obvious and palpable dislocation or fracture of the coccyx as a result of a blow, kick, or fall. Infection after operation for pilonidal cyst may result in chronic pericoccygitis, and acute sacrococcygeal arthritis has been seen following trauma, exposure, and acute upper respiratory infections. An ankylosed coccyx may be broken during delivery, especially if a narrow pubic arch forces the fetal head to ride through the posterior triangle of the outlet. But we have known this to occur many times with coccygodynia an infrequent sequel, whereas the latter has been frequently seen after falls and external violence. In our experience, if a palpable deformity exists in association with coccygodynia, it is a forward dislocation of the coccyx, almost never a posterior luxation. Horseback riding is usually mentioned with the etiologic factors. The only such case in our experience occurred in using a mechanical gymnasium horse.

Neuralgia and Neuritis of the Coccygeal Plexus.—The third and largest group of the coccygodynias is that comprising neuralgia and neuritis of the coccygeal plexus. This formed over 60 per cent of the fifty-three patients studied for this condition. Such patients are those without history or findings of gross or discoverable injury to the coccyx, and who have neither organic nor psychogenic factors operating which would label the pain as reflex.

Neuralgia exists when there has been transient injury of the overlying coccygeal tissues, as in parturition, with subsequent inflammatory reaction, edema, and secondary fibrosis resulting in pinching, pressure or chronic irritation of the highly susceptible plexus. If the local condition is severe or suppuration occurs or the damage to the nerves is great, an actual neuritis supervenes, with the chance of spontaneous cure less.

Clinically, neuralgia and neuritis of the coccygeal plexus are sharply differentiated from the traumatic group. In the reflex type, the history and examination show an anorectal or systemic affection without tenderness or pain definitely localized in the coccygeal region. In the traumatic type, there is usually obvious or palpable deformity with aggravation of the pain on coccygeal motion. However in the neuralgic or neuritic type, while passive motion of the coccyx may be entirely painless, contraction of the levator ani muscle, stool evacuation, pinching the tissues at the tip of the coccyx, pressure on the ventral coccygeal surface or over the sacrococcygeal joint, may induce exquisite pain, reproducing that for which the patient seeks relief. The pain is well localized to the anococcygeal body. When there is pain radiation into the back, buttocks, or legs, some other causative condition must be sought for. It is only in reflex coccygodynia that there is notable pain radiation.

It is highly important not to adjudge a patient with true coccygodynia of the traumatic or neuralgic types a psychoneurotic because of nervous manifestations developing in the course of the illness. The marked disability from continuous or recurrent pain is conducive to changes suggesting nervous imbalance, especially in those with low pain tolerance. Psychiatric therapy can hardly be effective when the primary factor continues to operate, although one cannot minimize the value of associated suggestive therapy.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Endocrinology

Balashova and Sicheva: Capillaroscopy in Some Endocrine Diseases, *Vestnic Endocrinol. (Moscow)* 5: 632, 1935.

The authors investigated by means of a capillaroscope the capillaries of the nail beds, the skin of the back of the wrist and the foot, and in some patients the skin of the forearm in cases of diseases of endocrine glands. In 40 cases of hypofunction of the ovaries atony of the capillaries was found and in the capillary loop the venous branch was dilated. The blood stream was slower and in the majority of loops there was stasis. The stream is not always homogenous, often there was a granular appearance. The subpapillary net was dilated. Clinically wrists were cyanotic, edematous, and moist. Fingers were large with short, thick and dim nails and very pale. *Cutis marmorata* was noted especially on the extremities.

In hypoplasia and aplasia of the sexual apparatus (early eunuchoidism), there was noted delay in the development of the ectodermal capillary net.

In cases of amenorrhea on the basis of general infantilism there was found a hypoplastic net of capillaries with a multitude of aneurysms.

There was a close similarity in the picture of the capillaries in the cases of obesity of hypophyseal-ovarian type, dystrophia adiposo-genitalis and obesity due to ovarian insufficiency. The outstanding characteristic for the majority of cases was unusually fantastic and a great variety of forms of capillaries due to their extreme tortuosity and large amount of aneurysm, long loops curled up; the blood stream was often slower than normal.

ALEXANDER GABRIELIANZ.

Werner, A. A.: Syndrome Accompanying Deficiency or Absence of the Ovarian Follicular Hormone, *Endocrinology* 19: 695, 1935.

This article is based upon an analysis of the objective signs and subjective symptoms presented by 197 women having deficiency or absence of the ovarian follicular hormone. This group of patients consists of 53 castrates, 96 women in the menopause and 48 subjects having involutional melancholia. The subjective symptoms are classified as nervous, circulatory and general. That these symptoms do accompany ovarian hypofunction or afunction is evidenced by their regularity of occurrence in 53 castrates studied. This same train of symptoms is found with striking parallelism in the menopause and involutional melancholia.

J. THORNWELL WITHERSPOON.

Goecke, Herman: The Action of the Male Sex Hormone (Testicular) at the End of Pregnancy, *Ztschr. f. Geburtsh. u. Gynäk.* 112: 273, 1936.

The author was able to demonstrate the presence of the male sex hormone in 71 per cent of the placentas of female fetuses examined. He was never able to detect

finger of the left hand is introduced into the rectum and the region is carefully palpated between it and the thumb externally. The shape and structure of the coccyx are determined and the position of the spot of greatest tenderness is carefully noted. This is usually at the tip of the coccyx, 1 cm. beyond the tip in the perineal body, or at the sacro-coccygeal joint. At first the entire area may be noted as tender, but a persistent search will locate one spot of exquisite tenderness. This marks the site of the first injection. The skin is sterilized with 3½ per cent iodine on a cotton applicator, and the injection made with the right hand, the fingers of the left hand remaining in situ to definitely locate and place the injection, as well as guard against rectal perforation. Three to 6 c.c. of 2 per cent novocaine solution are used for the initial injection, and repeated every five to seven days until complete relief is obtained. Four injections usually suffice. If the coccygodynia is sharply localized to a spot in the perineal body, ½ c.c. of 2 per cent novocaine is injected, followed in a moment, without withdrawing the needle, by 1 or 1.5 c.c. of 80 per cent alcohol. Where the pain is localized on the ventral surface of the coccyx, the extreme lithotomy position will permit insertion of a long needle through the perineal body past the tip of the coccyx and into the coccygeal plexus. The injection may also be made through an approach on either side of the coccyx. One may elect to seal the injection site with collodion, but this is not necessary. The patient is instructed to take mineral oil or petroleum-agar emulsions, continue a usual diet, and employ sitz baths or hot oil enemas to relieve the aching pain or soreness occasionally experienced.

No serious complications will result if the above instructions as to type, amount, and placement of injections are followed. The two very severe reactions in 53 patients were due to injection overdosage of alcohol.

The results are excellent. In this series, 41 were clinically cured. Ten did not complete the series and of these, 6 later reported marked improvement. Four were not traced. Two patients received severe reactions, refused further treatment, and are recorded as having been adversely affected by treatment.

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tumor should be enucleated. If no tumor is discovered in the pelvic region, lumbar region, or hypophyseal area, the treatment is much more difficult. The author suggests various forms of hormone therapy, depending upon the endocrine organ or organs suspected as being responsible for the virilism.

J. P. GREENHILL.

Ahumada and Calatroni: Arrhenoblastoma of the Ovary, *Bol. Soc. de obst. y ginec.* (Buenos Aires) 15: 488, 1936.

The patient prior to removal of the ovarian tumor had marked masculine distribution of hair, with a male figure, and marked elongation of the clitoris. Soon after removal of the arrhenoblastoma the masculine characteristics began to diminish and now, after a period of four years, female characteristics predominate.

MARIO A. CASTALLO.

Falkiner, Ninian McL.: Relation of the Ovarian Cycle to Endocrinology, *Brit. M. J.* 1: 149, 1936.

The author presented eight specimens of human corpora lutea removed at different stages in the menstrual cycle and attempted to correlate the significance of hemorrhage into the corpus luteum. This hemorrhage, the author claims, is synchronous with the bleeding from the uterine mucosa of menstruation. In the corpus luteum of pregnancy no such gross hemorrhage could be demonstrated.

"The administration of luteal extracts in the present state of our knowledge is not of great clinical use." The author believes, however, that the administration of progestin in cases of threatened and repeated abortion may be useful. The corpus luteum extract may produce a satisfactory condition for embedding the ovum, and it may help to maintain the early decidua in a condition suitable for the development of the placenta. It may also aid in reducing the liability of abortion by reducing the irritability of the uterine muscle, making it less likely to undergo contractions. Further studies in this field are essential.

F. L. ADAIR AND S. A. PEARL.

Ehrhardt, K., and Fischer-Wasels, H.: Study of the Content of Corpus Luteum Hormone in the Human Placenta, *Monatschr. f. Geburtsh. u. Gynäk.* 102: 80, 1936.

The authors found that the amount of corpus luteum hormone in the mature human placenta is inconstant and small, having been found only in 8 per cent of the cases studied. However, this hormone was present more frequently in immature placentas of women between the sixth and eighth months of pregnancy. No hormone could be found in placentas of pregnancies less than four months old. Extracts of placentas from patients with eclampsia and preeclampsia gave positive results for the hormone but no conclusions should be drawn from this concerning the etiology of the toxemias of pregnancy.

The parenteral administration of corpus luteum hormone failed to lead to the detection of the hormone in the urine. Hence this hormone like the follicle hormone is inactivated in the body. The corpus luteum extract had a marked stimulating effect on the breasts of infantile rabbits.

The studies of the authors are of practical significance because they show which placentas are useful for their corpus luteum hormone effect. The most valuable placentas are those obtained at the sixth, seventh, and eighth months of gestation, after which came those of the fifth and ninth months. In two cases of habitual

the hormone in the placentas of male fetuses. In the case of twins of opposite sex, the placenta of the female only contained the male sex hormone. He believes that the male hormone is utilized by the male fetus in intrauterine life, and therefore is absent in the placenta. In the cases of hydatiform mole no male hormone was demonstrable in the cystic masses found in the uterus. The urine of these patients contained large amounts of the hormone. From this fact the author concludes that there is no definite relationship between the amount of hormone found in the placenta and the amount excreted in the urine. He also found that the male sex hormone was present in the urine at the end of pregnancy only when a male child was to be born and never when the child was to be a female. This is explained as follows: Although the placenta of a male fetus produces large amounts of the m.s.h., it quickly passes into the blood stream, because of the great requirements of the fetus, and is excreted in the urine. The female fetus does not require the hormone for its own use, so that it remains stored up in the placenta, and is not found in the blood stream or in the urine. The author believes that the sex of the unborn child can be determined in at least 80 per cent of the cases, for in that number a minimum of one cock unit of hormone is present in three liters of urine in the case of a male child, whereas none, or at least less than one cock comb growing unit, is present in a similar amount of urine in the case of a female child.

E. S. AUER.

Deanesly and Parkes: Oestrogenic Action of Compounds of the Androsterone-Testosterone Series, *Brit. M. J.* 1: 257, 1936.

Extracts of testis and male urine contain estrogenic substances of the estrone group. It is now recognized that substances similar in chemical nature to estrone may have some degree of estrogenic power. It has been possible to hydrogenate estrone, which itself shows no male hormone activity, to a substance having male hormone activity but no estrogenic power. The first male hormone obtained, androsterone, isolated from male urine was nonestrogenic by the vaginal cornification test and by a plumage test. Recently Butenandt and Kudzsus reported that trans-dehydroandrosterone, androstenedione, and testosterone cause opening of the vagina in the intact immature rat. Trans-dehydroandrosterone is present in male urine. Androstenediol increases the size of the uterus and vagina of the adult ovariectomized rat. It seems likely that the estrogenic action of testis and male urine extracts may be due to the presence of compounds exerting an estrogenic action, rather than the actual presence of estrone or some other purely estrogenic compound.

F. L. ADAIR AND S. A. PEARL.

Seguy, J.: Virilism Among Puberal Women, *Gynéc. et obstét.* 33: 215, 1936.

Virilism in women is characterized by two groups of symptoms. First there is regression of secondary feminine sexual characteristics such as the disappearance of menstruation, atrophy of the breasts, and loss of fat in various parts of the body. On the other hand, secondary masculine sex characteristics appear. For example the clitoris enlarges, the voice becomes masculine and the general body contour changes. Virilism, therefore, consists essentially of changes in the secondary sex characteristics without involvement of the primary sex organs. It is due to a disturbance in one or more glands of internal secretion. The chief type of ovarian disturbance which is responsible for virilism is arrhenoblastoma of the ovary. Virilism may also be caused by corticosuprarenal lesions, anterior hypophyseal disturbances and thyroid diseases. The treatment of virilism varies considerably. If a unilateral ovarian tumor is found it should be removed, likewise a tumor of the suprarenal gland. If x-ray pictures demonstrate a tumor of the hypophysis this

took place giving a H-ion concentration of 5. A similar but less abrupt change of flora and vaginal acidity associated with normal puberty in girls has been described by Socken.

The results of similar observations on children, briefly detailed, indicate that this response to the injection of estrin may explain the favorable results which have been reported in the treatment of infantile gonorrheal vaginitis.

J. THORNWELL WITHERSPOON.

Hisaw, Frederick L., and Lendrum, Frederick C.: Squamous Metaplasia in the Cervical Glands of the Monkey Following Estrin Administration, *Endocrinology* 20: 228, 1936.

The authors have confirmed the observations of Overholser and Allen, and of Engle and Smith, that prolonged estrin stimulation produces in the cervix of the monkey a condition of squamous cell metaplasia which resembles beginning malignancy in the human female. Stimulation of the monkey's own ovaries to produce estrin by administration of anterior pituitary preparations is usually not followed by squamous metaplasia. Simultaneous corporin therapy will inhibit the action of estrin in evoking squamous metaplasia in the cervix. The cervical lesions apparently undergo regression, either spontaneously when all treatment is withdrawn, or under the influence of corporin even when estrin is continued.

J. THORNWELL WITHERSPOON.

Dallera, Nicolo: Modification of Uterine Epithelium Under Hormonal Influences, *Folia gynaec.-demogr. (Genova)* 33: 8, 1936.

The author describes the histologic modifications of the uterine mucosa of rats, during the stage of prolan A blood saturation and during the injections into these animals of folliculin. He discusses on the basis of the alterations observed, experimental hormonal conditions which give rise to the marked epithelial transformations observed, and those which occur normally in women during those years when carcinoma of the uterus is more prevalent.

The author makes a plea for further studies along this line, in order that the cause of carcinoma may be better approached.

MARIO A. CASTALLO.

Damm, P. N.: Examination of the Changes in the Uterine Mucosa Following Excessive Doses of Follicular Hormone, *Acta obst. et. gynec. Scandinav.* 15: 58, 1935.

In a twenty-nine-year-old castrated woman treated with 750,000 M. U. of follicular hormone, Damm observed changes in the atrophied endometrium which correspond to glandular-cystic hyperplasia. From this experience the author warns that large doses of follicular hormone should not be used on patients with deficient or inactive ovaries unless followed up by treatment with progestin.

J. P. GREENHILL.

Witherspoon, J. Thornwell: Hormonal Origin of Endometrioma, *Arch. Path.* 20: 22, 1935.

Witherspoon advances the hypothesis that the igniting factor which stimulates the endometrial implant to proliferation is the ovarian follicular hormone. The morphologic and functional characteristics of an endometrioma and of the uterine endometrium are similar; the integrity and function of the endometrioma are

abortion the authors succeeded in maintaining the pregnancies to term by giving extracts of placentas obtained from the sixth and seventh months. In cases of uterine hypoplasia, a definite growth of the uterus could be obtained with placental extracts.

J. P. GREENHILL.

Guldborg, E.: Sites of Production of the Sex Hormones in Normal Pregnant Women in the Light of Hormone Analysis After Oophorectomy During Pregnancy, Acta obst. et gynec. Scandinav. 15: 343, 1936.

A critical survey of the literature indicates the correctness of Halban's theory, first promulgated in 1905, that the placenta is the seat of hormone production during pregnancy. Particular emphasis must be placed on the increasing number of reports of cases in which bilateral oophorectomy is performed early in pregnancy without interrupting the gestation. This indicates the wholly subordinate rôle played by the ovary. The fetus likewise is not important for maintenance of the pregnancy as evidenced by the continued development of gestations in the presence of hydatid moles.

Hormone studies during pregnancy in women whose ovaries were removed have proved that folliculin, the corpus luteum hormone and the gonadotropic hormones are produced in the placenta. There is a biologic difference between the follicle maturing hormone secreted during pregnancy and in the castrated state.

J. P. GREENHILL.

Bandler, U: Gonadotropic Hormones in the Urine of Women With Tumors, Monatschr. f. Geburtsh. u. Gynäk. 102: 156, 1936.

In a series of 21 women who had squamous cell carcinoma of the cervix, Bandler found gonadotropic hormones in the urine in 72.7 per cent before treatment was instituted. The amounts of hormone varied between 80 and 500 mouse units per liter of morning urine. After the first x-ray treatment there was a decrease in the amount of hormone in the urine. The level rose before the second treatment and then again decreased. In untreated cases of adenocarcinoma of the cervix, these hormones could be found in only half of the cases. The hormones were found in 78 per cent of untreated women with squamous cell carcinoma of the vulva. They could not be detected or only in very small amounts in women who had benign tumors and gynecologic illnesses.

J. P. GREENHILL.

Vincent, B., and Lewis, Robert M.: The Induction of an Acid Vaginal Secretion in the Immature Macaque by Injection of Estrin, Endocrinology 20: 210, 1936.

In 6 immature macaques pH determinations proved the vaginal fluid to be definitely alkaline. Three monkeys were then injected over a period of two weeks with sufficient estrin to cause reddening of the sexual skin and to produce hyperplasia of the vaginal mucosa.

The vaginal fluid of the injected animals was found to be highly acid. An increase in the H-ion concentration of at least 2 pH units was observed in each case. After withdrawal of the hormone and the subsequent return of the vaginal mucosa to the condition normal for the immature animal, the vaginal fluid was found to return to its former alkalinity.

In one animal the vaginal fluid showed pH 7.8 forty-eight hours before reddening of the sexual skin occurred. With the discoloration an extraordinarily rapid shift

Mortimer, Wright, and Collip: *The Effect of Oestrogenic Hormones on the Nasal Mucosa; Their Rôle in the Naso-Sexual Relationship; and Their Significance in Clinical Rhinology*, *Canad. M. A. J.* 35: 615, 1936.

A review of the literature on the behavior of the conchal mucosa in relation to the sex cycle is given. A comparison of the nasal cavities of the human and monkey is made and individual variations are indicated. A careful control in the series of 28 monkeys, which were studied, is described. A rhinologist examined the nasal cavity weekly without individual identification or knowledge of the menstrual cycle. The menstrual cycle of monkeys was recorded by others. It was ascertained that the estrogenic hormones exert definite influence upon the conchal membrane. Crystalline estrone and estriol and emmenin produce redness and swelling similar to the changes in other sex-skin areas. This is obtained also in castrated animals and in males.

Studies next were begun in women. It is apparent that the hormones of the ovary exercise a specific physiologic influence upon the mucous membrane of the conchae. Thus it is evident why the rhinologist should bear in mind the possible alteration of the mucosa from factors other than primary rhinitis, such as pregnancy and various stages of the menstrual cycle. Finally, estrogenic hormone substances may be employed in certain cases of atrophic rhinitis and are thus of particular interest to the rhinologist.

H. CLOSE HESSELTINE.

Friedgood, H. B., and Pincus, G.: *Nervous Control of the Hypophysis*, *Endocrinology* 19: 710, 1935.

Thirty-two adult female rabbits were isolated in separate cages for a period of three to four weeks before being used in the present investigation. Faradic stimulation of the cervical sympathetic nerves was carried out in 6 of these animals, while 3 of them (controls) were subjected to the same operative procedures up to but not including the stimulation of their cervical sympathetics. The remaining 23 rabbits (also controls) were sacrificed after their period of isolation. None of the controls showed either ovulation or microscopic evidence of ovum maturation; whereas each of the 6 rabbits which had their cervical sympathetics stimulated revealed extensive maturation of their ova, and ovulation occurred in 3 of them. It is concluded from these results that the rate of secretion of the gonadotropic principle can be experimentally increased by faradic stimulation of the sympathetic fibers which innervate the anterior hypophysis. These experiments also indicate that the cervical sympathetic nerves may be at least partially responsible during coitus for stimulating the anterior hypophysis to release its gonadotropic secretions in increased amounts.

J. THORNWELL WITHERSPOON.

Zondek, Bernhard: *The Inhibitory Effect of Follicular Hormone on the Anterior Lobe of the Pituitary Gland*, *Lancet* 1: 10, 1936.

This report indicates that the follicular hormone inhibits the hormonal function of the anterior pituitary. Infantile rats were used and controls carefully made. The preparation was given subcutaneously twice a week as a-hormone in aqueous or oily solution, or the benzoic ester of dihydrofollicular hormone (Dimenformon). The control animals received injections of normal saline or olive oil. When 100 M.U. were given no effects on body growth resulted, but when 1,000 M.U. twice a week were given definite inhibition of growth occurred.

The prolonged application of the hormone induces a continuous estrus. The vagina and uterus enlarge and the lining membranes proliferate. Abundant corpora lutea are found in the control animals but they are absent in the treated

dependent on the presence of active ovarian tissue; the endometrioma gives a decidual reaction during pregnancy and undergoes the phases of the menstrual cycle. It therefore appears highly probable that the estrogenic principle is essential for the maintenance of the lesion. In 64 per cent of 44 cases studied it was found that ovarian and uterine endometriomas were associated with endometrial hyperplasia, a figure too high to indicate a mere coincidence. Not only are the uterine and the aberrant endometrium stimulated to hyperplasia and tumor proliferation, but the uterine musculature also is affected. Functional uterine hemorrhage and sterility that are associated with endometrioma may also be explained and accounted for according to this hypothesis. The frequency of sterility (60 per cent) with endometrioma is due to the presence of multiple follicular cysts of the ovaries in the absence of ovulation and of the formation of corpora lutea.

W. B. SERBIN.

Tapfer and Haslhofer: Enlargement of the Pelvis by Means of Hormones in Animal Experiments, Arch. f. Gynäk. 159: 313, 1935.

The authors discuss the considerable expansion of the pelvis which takes place in pregnancy from a relaxation of the symphyseal and sacroiliac joints as the result of hormonal stimulation. All investigators agree that such expansion is due to hormonal influences, but nobody has as yet determined exactly which hormone is responsible for such joint changes.

The authors used the blood serum of pregnant rabbits in nonpregnant guinea pigs and observed dilatation and relaxation of the pubic joints which grossly and microscopically were exactly the same as those produced by pregnancy. The nearer term the rabbit was, from which the serum was taken, the greater was the joint reaction. The intensity of the reaction does not, therefore, follow the degree of corpus luteum hormone concentration but rather that of estrin. Apparently the estrogenic hormone produces these characteristic joint changes. The authors also experimented with commercially prepared hormones and again found that the estrogenic hormone caused these characteristic changes.

RALPH A. REIS.

MacDonald, Ian G.: The Response of the Mammary Gland to Prolonged Stimulation With Ovarian Hormones, Surg. Gynec. Obst. 63: 138, 1936.

The continuous administration of the ovarian hormone estrin in castrated rabbits produces, at first, a generalized overgrowth and ramification of the ductal system in the mammary gland with practically no acinar growth.

Carried further (100 days), little gross change occurs, but atypical histological variations appear in the ductal epithelium which often verge on the borderline of neoplastic changes.

When such stimulation is prolonged for six months or more, both the gross ductal growth and microscopic epithelial hyperplasia regress to a nearly resting state. Ductal widening is not prominent under pure estrin stimulation.

In rabbits the response of the ductal system of the breast and its epithelium to continuous estrin stimulation is confined to certain limits, past which a refractory state is set up.

Estrin and corpus luteum extract in combination produce both ductal and acinar overgrowth; early secretion occurs and the ducts become distended.

Dilation of the ducts is probably mechanical from distention by secretion, and not a specific effect of estrin.

Estrin and progestin, on the basis of present evidence, do not produce specific pathologic lesions, cystic disease and adenosis.

WM. C. HENSKE.

Karlík, L. N.: Rare Case of Pregnancy and Delivery in an Hypophysectomized Bitch, *Vopr. Endocrinol. (Moscow)* p. 809, 1936.

Contrary to the belief of all experimental workers that pregnancy cannot take place in the hypophysectomized animal, the author reports a case of a grown bitch of 7 kg. on which hypophysectomy was performed on Oct. 19, 1932 through the temporal route. The dog increased in weight shortly to 8.5 kg. On March 15, 1933, the right lobe of the thyroid gland and the right parathyroid glands were removed. Later on the bitch was kept with other hypophysectomized dogs of both sexes for five or six hours daily. Feb. 3, 1934, 478 days after hypophysectomy, the bitch gave birth to one puppy. The puppy suckled vigorously, but died the next day. On autopsy every organ, including the skeletal and muscular systems, were found normal. The stomach was absolutely empty. In the mother's mammary glands, no traces of milk were found. April 13, 1934, the bitch died in an experiment with the injection of insulin. The autopsy confirmed the absence of the hypophysis.

ALEXANDER GABRIELIANZ.

Fagioli, Mario: X-Ray Study of the Cranium in Women With Ovarian Dysfunction, *Ginecologia (Torino)* 6: 625, 1935.

On the basis of radiographic studies on twenty-four women the author affirms that in the presence of secondary ovarian insufficiency the sella turcica appears in variable forms and usually is larger. In these cases also calcification of the pineal body is frequently noticed.

AUGUST F. DARO.

Thaddea, Sigismund: Relationship Between Adrenal Cortex and the Gonads, *Ztschr. f. Geburtsh. u. Gynäk.* 110: 225, 1935.

The author believes that the hormones of the adrenal cortex influence gonadal function by way of the anterior lobe of the pituitary, as well as regulate the metabolism of carbohydrates. He also demonstrates a close relationship between the hormones of the adrenal cortex and vitamin C. During pregnancy there is an increased demand for the hormone of the adrenal cortex. In cases of pregnancy associated with Addison's disease there is an increased sensitivity to toxins. Hyperemesis and adynamia are markedly increased in severity. In these cases sodium chloride therapy is indicated because both conditions cause a loss of blood chlorides. In severe cases of Addison's disease complicated by pregnancy, the latter must be terminated because administration of adrenal cortex extract does not stop the progression of symptoms. Mild cases may be carried to term with proper treatment with adrenal cortex hormones.

EUGENE S. AUER.

Books Received

ERGEBNISSE DER MEDIZINISCHEN STRAHLENFORSCHUNG. Herausgegeben von Holfelder, Holthusen, Juengling, Martius und Schinz. Band VII. 622 Seiten mit 294 Abbildungen im Text. Verlag von Georg Thieme, Leipzig, 1936.

FILLE OU GARÇON. Par Docteur Jules Regnault. Editions Medieis, Paris, 1936.

THE EGGS OF MAMMALS. By Gregory Pincus, Assistant Professor of General Physiology, Harvard University. 160 pages, illustrated. The Macmillan Company, New York, 1936.

ones. The ovaries are retarded in their development. The male genital organs are completely arrested in their development by folliculin. The larger the amount of hormone the greater the inhibition of growth. "Follicular hormone paralyzes the gonadotropic hormones of the anterior pituitary—and seemingly the luteinizing hormone, prolan B, in particular—thus hindering them from exerting their normal influences on the ovaries."

H. CLOSE HESSELTINE.

Zondek, Bernhard: Impairment of Anterior Pituitary Functions by Follicular Hormone, Lancet 2: 842, 1936.

The ovarian function depends upon the gonadotropic hormones of the anterior lobe of the pituitary. Small doses of estrin stimulate the function of the anterior lobe while large ones depress it. In the animal (rat and chicken) small amounts produce proliferation of the uterine mucosa, but large amounts cause cystic hyperplasia and ultimately destruction, necrosis and aseptic suppuration.

Because the growth hormone balance is affected later, the cells producing gonadotropic hormone are the more sensitive. The growth is altered by action upon the bone growth. The follicular hormone does not inhibit the mechanism of production but only the mechanism of secretion. Hence the anterior pituitary functions are not equally and simultaneously affected. Growth is not resumed after several months of estrin treatment unless Evans's pituitary growth hormone is administered, which proves that the dwarfing was of pituitary origin. Moreover, the follicular hormone does not inhibit the production of the gonadotropic hormones in the anterior lobe cells but only prevents them from entering the blood stream.

The experimental animal differs significantly from the hypophysectomized one.

H. CLOSE HESSELTINE.

Jones, M. S., and MacGregor, T. N.: Inhibitory Effect of Follicular Hormone on the Anterior Pituitary in Humans, Lancet 2: 974, 1936.

The authors attempted to inhibit the gonadotropic and the diabetogenic principle of the anterior pituitary by giving large doses of estrin. The ten experimental subjects were all chronic psychotic patients between the ages of fifty-two and eighty-three (average 62.6). Metabolic and endocrine fluctuations due to emotional causes were improbable. The amount of gonadotropic hormone in the urine and a sugar tolerance curve were established before administering 500,000 to 1,000,000 M.U. estrin (Dimenformon) in a period of twenty days. Seven of the ten women had bleeding from the uterus. The psychopathic state remained unaltered.

This procedure caused the excretion of the gonadotropic hormone, which had exceeded 50 M.U. per liter, to be abolished. No consistent effect on the glucose tolerance test resulted.

H. CLOSE HESSELTINE.

Zondek, Bernhard: Tumour of the Pituitary Induced With Follicular Hormone, Lancet 1: 776, 1936.

Under administration of follicular hormone to animals the gonads underwent complete atrophy while the pituitary enlarged in all cases of males, but macroscopically remained unaltered in the females. The functional inhibition of the anterior lobe of the pituitary appeared equally in males and females. The growth of the pituitary is not responsible for this change.

The author produced dwarfed animals with hypoplastic genitals by prolonged administration of follicular hormone.

H. CLOSE HESSELTINE.

CARCINOMA OF THE FEMALE GENITAL ORGANS. By M. C. Malinowsky and E. Quater. Translated from the Russian by A. S. Schwartzmann, M.D. Illustrated, 255 pages. Published by Bruce Humphries, Inc., 306 Stuart Street, Boston, Mass.

CHILDLESS. A Study of Sterility, Its Causes and Treatment. By Sam Gordon Berkow, M.D. Illustrated, 307 pages. Published by Lee Furman, Inc., 381 Fourth Ave., New York City, 1937.

KIDNEY PAIN, Its Causation and Treatment. By J. Leon Jona, M.D., F.R.A.C.S., Hon. Asst. Gynaecological Surgeon, Women's Hospital in Melbourne. Illustrated, 94 pages. J. & A. Churchill, Ltd., London, 1937.

Items

American Board of Obstetrics and Gynecology

Practical oral and clinical examinations for Group A and B applicants will be held at Atlantic City, N. J., on June 7 and 8, 1937.

Applications for the Group A examination will be received in the office of the Secretary, Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6), Pa., to April 9, 1937. Application blanks may be secured from the Secretary's office.

Washington Gynecological Society

The following officers were elected at the meeting held May 26, 1936: *President*, Dr. Prentiss Willson; *First Vice-President*, Dr. Jerome F. Crowley; *Second Vice-President*, Dr. Henry L. Darner; *Treasurer*, Dr. Radford Brown; *Historian*, Dr. John W. Warner; *Secretary*, Dr. Herbert P. Ramsey; *Council Member*, Dr. William J. Stanton (term expires 1940) and continuing on the *Council* are Drs. J. J. Mundell, J. Kotz, A. E. Pagan, and the retiring president, Dr. E. W. Titus.

PROSTITUTION. By Tage Kemp, M.D., Copenhagen. Translated from the Danish by Elsie-Marie Werner Kornerup. 253 pages. Levin & Munksgaard, Copenhagen, 1936.

GYNECOLOGY AND OBSTETRICS. By Edwin M. Jameson, M.D. Surgeon, General Hospital, etc., Saranac Lake, N. Y. 170 pages with 5 illustrations. Paul B. Hoeber, Inc., New York, 1936.

DIE BEKAEMPFUNG DER EKLAMPTISCHEN SCHWANGERSCHAFTS-ERKRANKUNGEN. Von Heinrich Siedentopf, Oberarzt der Universitaets-Frauenklinik zu Leipzig. 86 Seiten. Johann Ambrosius Barth, Leipzig, 1936.

THERAPEUTICA DAS SYNDROMES GRAVIDO-PUERPERAES. Par Dr. Joao Pereira de Camargo, livre docente de medicina da Universidade do Rio de Janeiro, etc. 2. a edição correcta e muito augmentada. 376 pages. Freitas Bastos, Rio de Janeiro, 1936.

FACTS AND FRAUDS IN WOMAN'S HYGIENE. By Rachel Lynn Palmer and Sarah K. Greenberg, M.D. 311 pages. The Vanguard Press, New York, 1936.

PHYSICIAN, PASTOR AND PATIENT. Problems in Pastoral Medicine. By George W. Jacoby, M.D. 390 pages, illustrated. Paul B. Hoeber, Inc., New York, 1936.

MEDICINE AND MANKIND. Lectures to the Laity delivered at the Academy of Medicine in New York. Edited by Jago Galdston, M.D. 217 pages. D. Appleton-Century Company, New York, 1936.

MEDICAL MORALS AND MANNERS. By Hubert Ashley Royster, M.D. 333 pages. Chapel Hill, The University of North Carolina Press, 1937.

DISEASES OF THE NEWBORN. By Abraham Tow, M.D. Adjunct Professor of Pediatrics, New York Polyclinic Hospital, etc. Illustrated, 477 pages, Oxford University Press, New York, 1937.

INTO THE UNIVERSE. The Story of Human Birth. By Alan Frank Gutmacher, Associate in Obstetrics, Johns Hopkins University. Illustrated, 366 pages. The Viking Press, New York, 1937.

UEBER DIE GEBURTSTRAUMATISCHEN SCHAEDIGUNGEN DES ZENTRALNERVENSYSTEMS. Von Dr. Med. H. Nevinny, Universitaets-Frauenklinik in Koenigsberg, Pr. Mit 8 Textabbildungen und 12 Tafeln, 87 Seiten. Ferdinand Enke, Stuttgart, 1936.

PÉRIODES DE FÉCONDITÉ ET DE STÉRILITÉ CHEZ LA FEMME. Par H. Vignes et M. Robey. 85 pages. Masson et Cie., Paris, 1936.

INHALATION ANESTHESIA. By Arthur E. Guedel, M.D. Associate Clinical Professor of Surgery (Anesthesia), University of Southern California School of Medicine. 172 pages. The Macmillan Co., New York, 1937.

OBSTETRICAL GUIDE. By Philips J. Carter, M.D. From the Obstetrical Department of Louisiana State University Medical Center, New Orleans, La.

LEHRBUCH DER FRAUENHEILKUNDE (in zwei Baenden). Von Professor Dr. W. Weibel, Vorstand der II. Universitaets-Frauenklinik in Wien. Erster Band: Geburtshilfe. Mit 849 zum Teil mehrfarbigen Abbildungen im Text und 16 farbigen Tafeln, 647 Seiten. Urban und Schwarzenberg, Wien, 1937.

other episode of spontaneous, painless bleeding occurred. A cupful of bright red blood containing a few clots was passed. Bleeding ceased when patient went to bed. Entered the hospital on following day.

Examination revealed no bleeding, mucous membranes of good color, blood pressure 120/86, temperature 37° C., pulse 90, respirations 20. The abdomen was distended by a term-sized fetus in L.O.A., head not engaged, fetal heart in L.L.Q., Hb. 65 per cent (S), R.B.C. 4.3 M, W.B.C. 10,200, blood group, Moss I, urine negative. The presumable diagnosis was placenta previa. No vaginal examination was made since it was felt that the patient's age, parity, the nonengagement of the head, and the desire to sterilize her indicated cesarean section as the best method of treatment, regardless of the degree of previa. When bleeding recurred in small quantity the following day, section was performed.

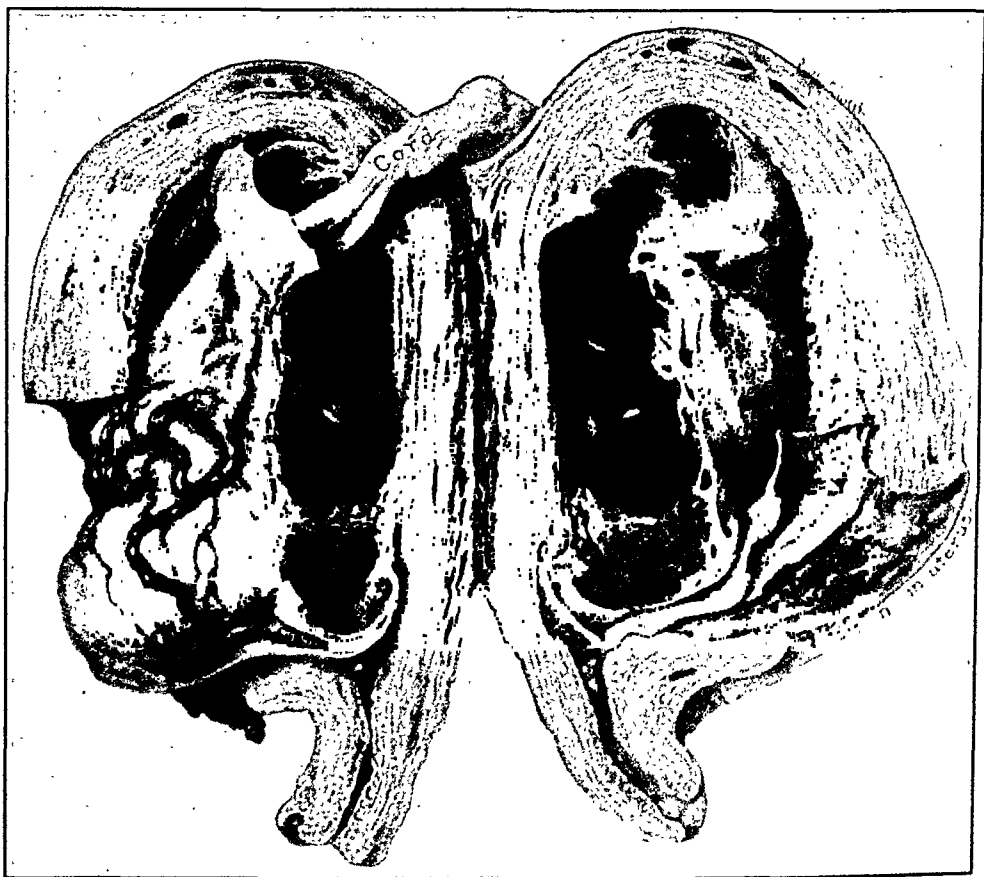


Fig. 1.—Fixed uterus opened sagittally in the midline. In this plane the placental margin is 2 cm. above the internal os. A circular sinus is present at the level of the internal os.

The vessels over the lower segment on the right side were more prominent than elsewhere, indicating probable implantation of the placenta in this region. Classical section was chosen in order to avoid these vessels. A normal female child weighing 3,670 gm. was delivered. In order to sterilize the patient and at the same time minimize the chance of infection, hysterectomy without removal of tubes or ovaries was chosen as the proper procedure. Before hysterectomy several sutures were placed to close the uterine incision, retaining the placenta in situ. Although it was planned to amputate through the lower portion of the cervix, the operator found that he had unintentionally opened the vaginal vault so that finally a total hysterectomy was done.

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Original Communications

ANATOMIC DESCRIPTION OF A CASE OF MARGINAL PLACENTA PREVIA

WITH A DISCUSSION OF THE ETIOLOGIC IMPLICATIONS

DANIEL G. MORTON, M.D., SAN FRANCISCO, CALIF.

*(From the Department of Obstetrics and Gynecology, University of California
Medical School)*

SINCE opportunities to study anatomically cases of placenta previa are very limited, it seems worth while to report the findings of a case which presented itself recently. The case in question is of interest not merely from the anatomic viewpoint but also because it embodies certain implications in regard to etiology, the frequency of the condition, and the cause of bleeding, none of which are exactly known at the present time.

CASE 1.—(No. 88252.) White, para v, aged forty years. Previous four pregnancies ended in full-term spontaneous deliveries without complications, in 1921, 1923, 1925, and 1927. Between the third and fourth pregnancies, she was curetted twice for bleeding, and may have had an abortion. Last menstrual period May 11, 1935. Estimated date of confinement Feb. 18, 1936. Patient entered the hospital Feb. 26, 1936, because of vaginal bleeding. She had registered in the prenatal clinic Jan. 18, 1936, a month short of term; she was seen at frequent intervals between then and hospital entry. Her course had been uneventful except for slight ankle edema. Pelvis normal, Wassermann negative, no significant physical findings except marked vaginal relaxation. On February 16, while preparing breakfast, patient suddenly felt blood trickling down her leg; no pain. About one-half glass dark red blood was passed. She went to bed immediately. During the next few days there was no further bleeding. On February 25, twenty-four hours before entry, an-

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the internal os, the membranes being reflected over the os and up on to the anterior wall. There was a small amount of old clotted blood between the internal os and the reflected membranes as well as in the cervical canal proper. The upper margin



A.



B.

C.

Fig. 3.—Sections showing decidua in cervix and lower segment. Areas from which these blocks were taken are indicated in Fig. 2. A, From middle of cervical canal. B, From upper part of cervical canal. C, From uterine wall just above internal os.

of attachment was on the posterior wall 13.5 cm. above the lower one. Two centimeters above the lower attachment the placenta was partially separated by blood

The patient made an uneventful recovery, the highest temperature being 38° C. on the second day. At discharge on the nineteenth postoperative day, her hemoglobin was 85 per cent, R.B.C. 4 M.

Description of Specimen.—(After fixation for twenty-four hours in 10 per cent formalin.) The specimen consisted of the entire uterus, including the cervix.

The uterus measured 21.5 cm. from tip of cervix to fundus, 16 cm. between tube portals, and 12 cm. in its greatest anteroposterior diameter. Low on the anterior wall was an 8 cm. incision held together by several sutures. The incision started 2 cm. above the level of the internal os and extended obliquely upward toward the

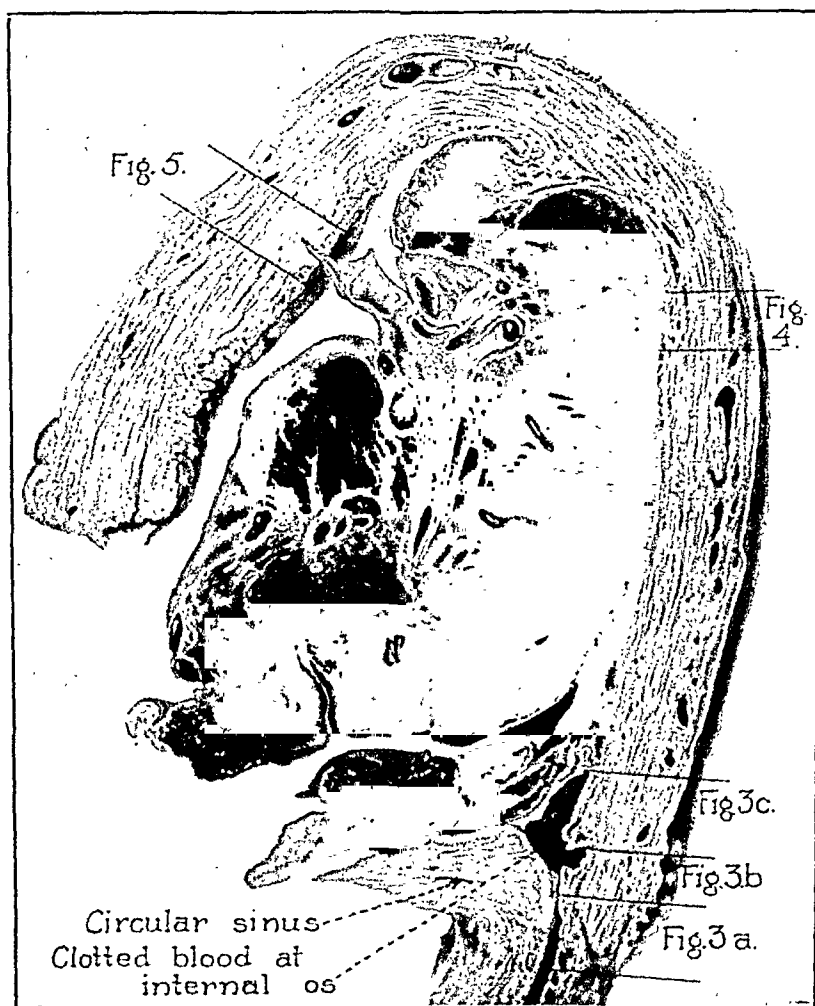
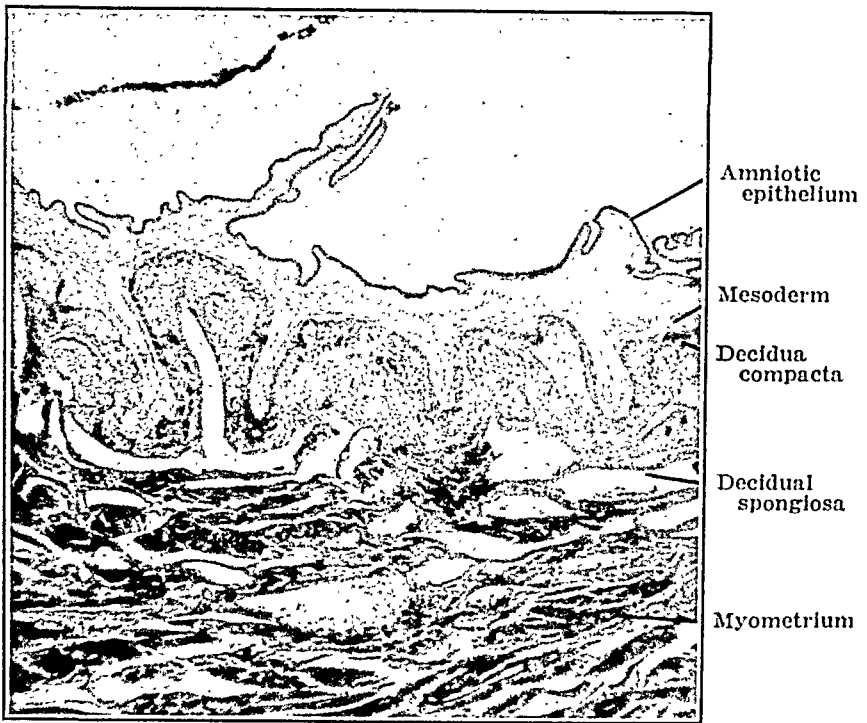


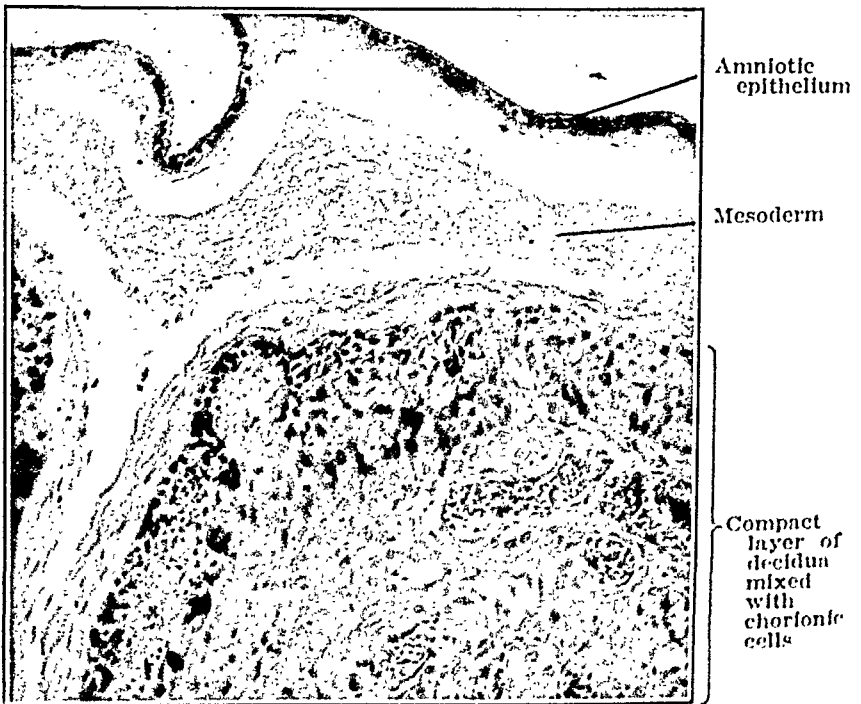
Fig. 2.—Segment cut sagittally 1.5 cm. to the right of the midline. The placental margin just reaches the internal os. Clotted blood is present in the upper part of the canal.

left cornu. From this incision protruded one margin of the placenta. The vessels on the anterior wall of the lower segment on the right side were much more prominent than elsewhere, indicating probable implantation of the placenta in this area. The cervical canal was intact, measuring 5 cm. from tip to internal os. On splitting the uterus in half in the sagittal plane (Fig. 1), the placenta was found implanted on the right posterolateral wall, so that about one-third remained in the left half of the uterus, two-thirds with cord attachment in the right half. A portion of the right margin of the placenta had already separated. The major portion remained attached. The lower margin of attachment in this plane was 2 cm. above

of the internal os. No old blood clung to this area, nor did it appear depressed, although this would actually be impossible unless a clot of considerable size had



A.

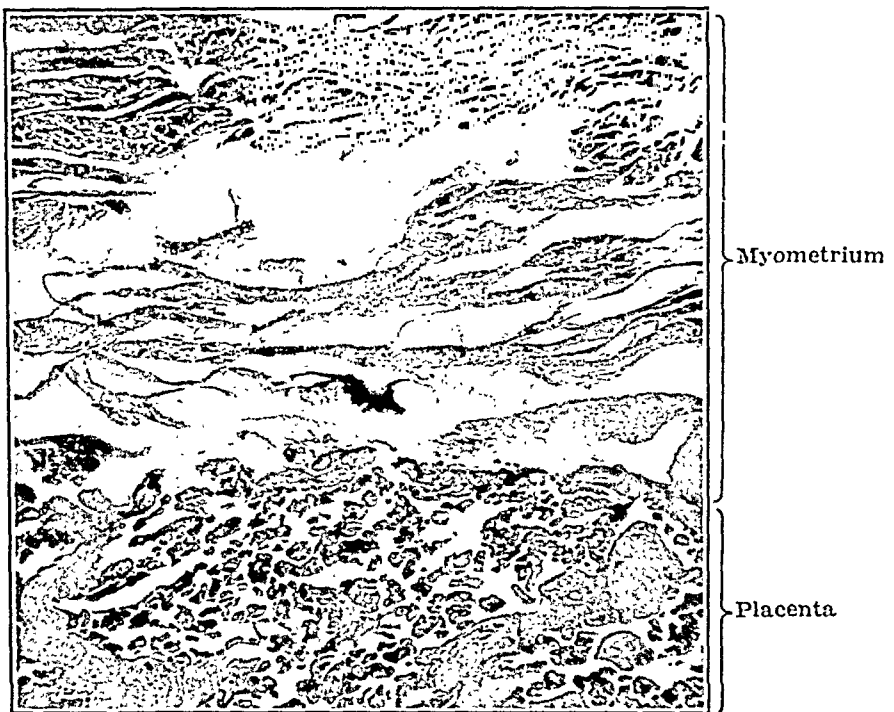


B.

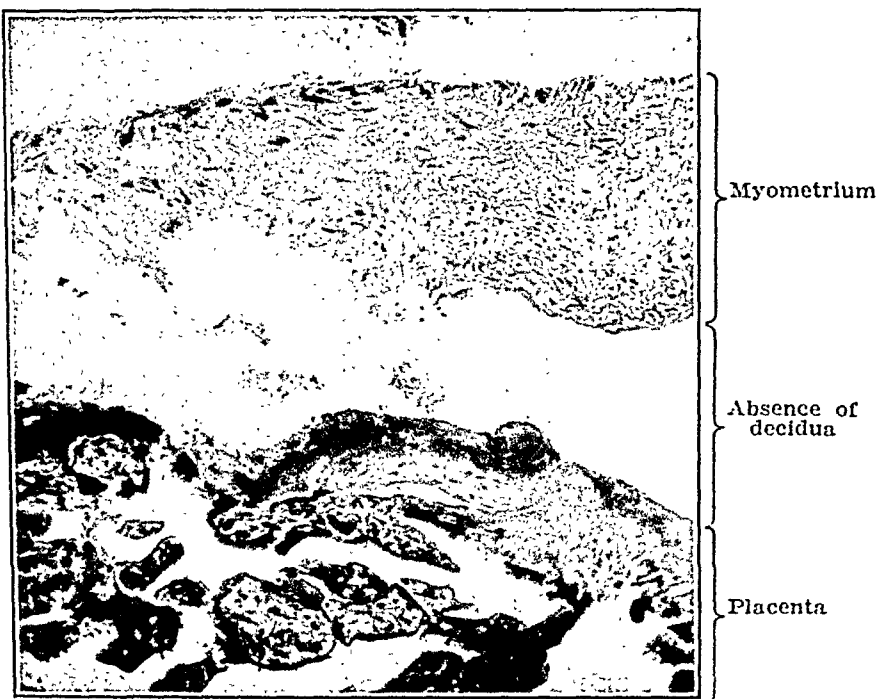
Fig. 5.—Sections showing decidua vera with membranes attached and thrown into numerous folds due to reduction in surface area incident to uterine contraction. Compact and spongy layers are well preserved. A, Low power; B, high power.

accumulated, since there was a cone-shaped space here which led into the cervical canal. The lower portion of this space *did* contain clotted blood. Fig. 2 represents

clot, otherwise it was uniformly attached (in this plane) by numerous membranous septa which divided this potential space into many varying sized sinuses, some as large as 2 cm. in diameter.



A.



B.

Fig. 4.—Section taken from a central point of the placental site. For exact location see Fig. 2. Illustrates the absence of decidua at a point where the amount normally is considerable. A, Low power; B, high power.

On elevating the lower border of the placenta in the right half, a margin of chorion frondosum was found extending from the right side just beyond the margin

site were larger and more numerous than elsewhere. A large circular sinus, 0.4 cm. in diameter, was situated in the middle of the wall at the level of the internal os. The decidua vera was distinguished as a flesh colored layer 0.75 cm. thick. With the membranes which remained adherent, it was thrown into many transverse folds. The decidua basalis was not distinguishable grossly as a definite layer. The inner one-fourth of the cervical wall was occupied by dilated cystic glands filled with mucus. The remainder of the inner half of the cervical wall was spongy and light in color. The outer half was darker, consisting of firm fibromuscular tissue.

Microscopic examination of blocks taken from the entire circumference of the uterine wall, in the sagittal plane, 1.5 cm. to the right of the midline, revealed several interesting findings. From the middle of the cervical canal upward to the placental margin, there was a distinct and quite well-marked decidual reaction (Fig. 3). Below this point the usual cervical structure was seen, the glands being dilated with mucus, the epithelium swollen. At the placental site the decidua was very scanty indeed. Fig. 4 is representative of the findings here, showing a section taken from the middle of the posterior wall, just above the central point of the placenta. The decidua here is represented by a lacy framework only, the spongy glandular layer. Almost nowhere in the basalis is the compact layer in evidence. In some areas even the spongiosa could not be made out (this, without placental separation). The decidua vera was much better preserved, both compact and spongy layers being clear and definite (Fig. 5). The intimate association of decidua vera and chorion laeve is well illustrated. This membrane, as well as the amnion, has been thrown into deep folds by the reduction in surface resulting from uterine contraction.

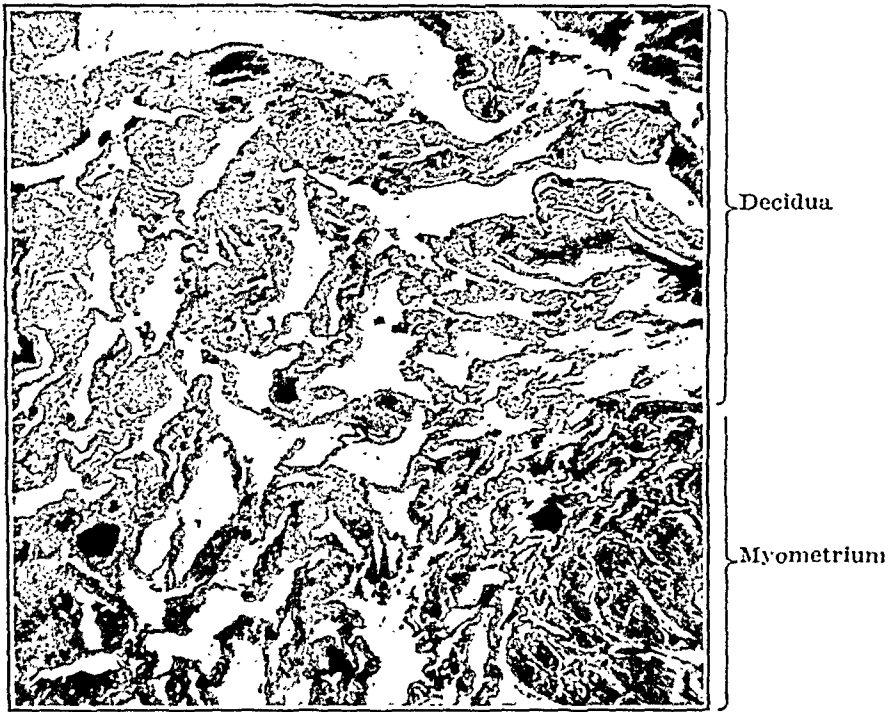
The placental tissue itself was normal in appearance, as was the cord. The most notable features microscopically are: (1) the large amount of decidual reaction in the cervical canal, and (2) the scantiness of decidua beneath the placenta higher up, where one would expect a marked decidual reaction.

DISCUSSION

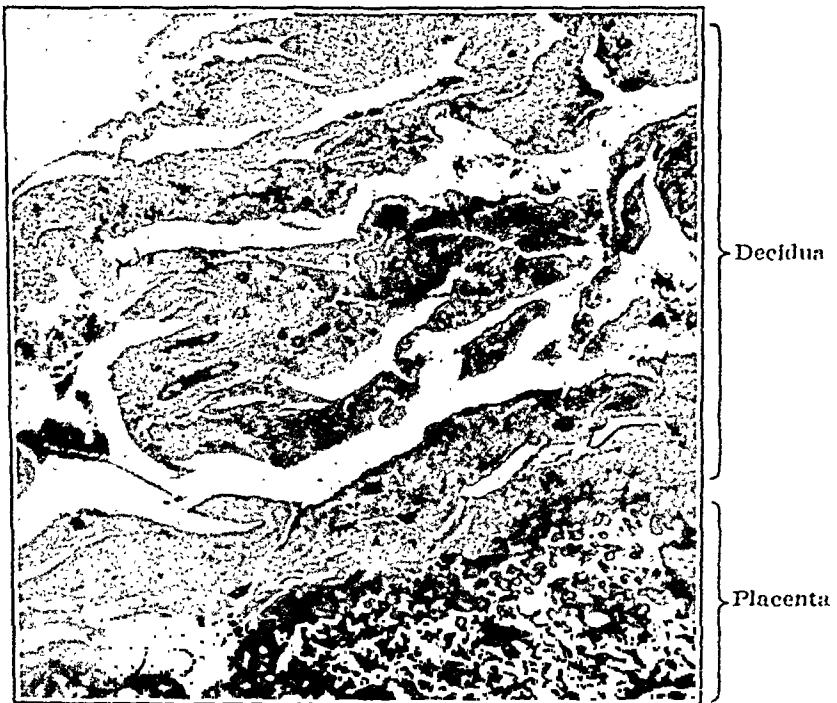
I shall not enter into a prolonged discussion of the etiology of placenta previa, but I do wish to correlate the findings in this case with several interesting and pertinent observations which have been made in the past. No one knows what determines the site of implantation of a fertilized ovum. It is known that the usual site is well up on the posterior or anterior wall, sometimes more or less laterally, very rarely in the fundus, and quite infrequently in the region of the cervix. These facts are in keeping with the anatomy of the pregnant uterus, in that the walls of the contractile portion of the uterus are lined by a thick layer of decidua, soil which presumably is ideal for implantation of the fertilized ovum and certainly prepared especially for it, whereas the decidual reaction in the segment of the uterus just above the cervix is usually scanty, and in the cervix itself entirely absent. What part gravity may play in determining a site low in the uterus is unknown, but in general is considered an inadequate explanation, though it may play a part in some.

In 1902 Strassmann¹ made a valuable contribution when he contended that low implantation might occur because of previous disease of the endometrium, thus making it unsuitable, or at least insufficient, for

a slab cut sagittally just 1.5 cm. to the right of the midline and shows clearly the placental margin covering the rim of the internal os.



A.



B.

Fig. 6.—Relative abundance of decidua beneath term placenta normally. A, Low power. From placental site of puerperal uterus just after placental separation. B, Low power. Decidua attached to term placenta.

The anterior uterine wall was 2.75 cm. thick, the posterior wall 2 cm. Dilated vessels and sinuses were prominent in the wall. Those underlying the placental

or disease of the placenta itself, nature's effort appears to be the same, i.e., to obtain adequate vascular connections for the placenta and fetus. Whenever the placenta does extend, the likelihood of the development of a previa becomes increased.

An entirely different mechanism was described by Hofmeier⁵ who showed definitely that *some* cases of placenta previa are due to a persistence of cotyledonous development on the capsularis or reflexa, the so-called reflexa placenta previa. When the capsularis has been carried out to the decidua vera and become fused with it, that portion having persistent villi may bridge the internal os; if the villi continue to develop, a definite previa will exist. This observation has been confirmed many times. However, as he himself admitted, this is only one cause of the condition. A number of definite cases of serotinal placenta previa have been described. The case described by Titus and Andrews⁶ in 1924 is a particularly good example of the serotinal variety.

Unfortunately the specimens which have been described have not been studied microscopically as thoroughly as they might have been, thus detailed information regarding the decidua is lacking. In my specimen, very striking features are the scantiness of the decidua basalis, and an abundance of decidual reaction in the cervix, suggesting that the cause of the condition was a defective decidua high in the uterus, a relative abundance low in the uterus. The amount of decidua beneath a term placenta, normally, is variable and may be quite scanty. However, in three term uteri removed at cesarean section, even after removal of the placenta, the amount of decidua at the placental site was definitely greater than that found beneath the still attached placenta of the case under discussion. Further, quite a considerable quantity of decidua can usually be distinguished microscopically in sections of term placentas (Fig. 6). Therefore, I believe that the observed findings furnish a distinct departure from the normal. The association of these findings with a placenta previa fits in with the theory of Strassmann, and tends to prove it a fundamental consideration in the etiology of this condition.

Study of this specimen also leads one to ponder the question of the frequency of placenta previa. Definitions of what constitutes a placenta previa vary. We speak of the central, partial or lateral, and marginal varieties—some designate these with respect to the undilated cervix, others with respect to the completely dilated cervix. It is obvious that as retraction and dilatation proceed, the relations of the placental margin and the opening in the uterus will change. Probably one should designate all cases as placenta previa in which the placental attachment is low enough in the uterus, so that obliteration of the cervical canal and dilatation of the os may cause some separation. A little reflection makes it evident, however, that in certain cases of lateral, or marginal placenta previa, in which the margin of the placenta does *not* reach the margin

the needs of the placenta by leading to defective vascularization. As he pointed out, this condition is associated with increasing age and parity and is more frequent in those having had rapidly repeated pregnancies. That is, it is more common in women in whom there has been a greater possibility of endometrial infection. All subsequent investigators have accepted Strassmann's view that previous endometritis or other abnormality of the endometrium plays an important rôle in the etiology of placenta previa. Although at the present time we do not recognize an endometritis which exists from month to month and year to year without causing definite symptoms, it is conceivable and probably true that permanent changes often *follow* endometrial infection or even pregnancy without succeeding infection. Many vessels become thrombotic at this time, thus diminishing the available vascular bed. With increasing age and parity these vascular changes with the accompanying fibrosis may become so widespread as to reach a point of paramount importance. It is certainly a common experience to find the uteri of older women, who have had numerous pregnancies, large, fibrotic, and containing many thrombosed vessels, conditions quite distinct from those found in the uteri of nulliparous women of the same age. Recently an interesting experiment was reported by Solomons and Canter.² Working with rabbits, they traumatized the lining of one horn of the uterus by passing a needle through it. Pregnancy was then allowed to occur. It rarely did so in the injured horn. If only a portion of a horn was injured, pregnancy often took place in the uninjured, but not in the injured portion. The theoretical observations of Strassmann and the experiments quoted suggest that the fertilized ovum attempts to find better soil if the lining of the corpus has been injured, inflamed, or has developed defectively for one reason or another.

Even after the placenta has located itself, it may spread out over a larger area if for some reason the soil is inadequate. It is well known that placentas from cases of placenta previa are frequently very extensive in area, though they may be quite thin. A particularly good example of this is illustrated in the specimen described by Thompson³ in 1921 which shows a central placenta previa, in which the placenta covers almost four-fifths of the uterine cavity; the entire placenta is below the insertion of the cord which is attached through the membranes and presumably indicates the original point of nidation. Further evidence of the placenta's ability to spread out is contained in Goodall's⁴ recent study of circumvallation of the placenta. He showed quite clearly how the placenta extends beyond its ordinary margins when there has been infarction or sclerosis, presumably as a compensatory mechanism. He further pointed out that the extension is opposite the area of infarction. To my mind, these observations furnish adequate proof of the placenta's ability to extend. Whether it be because of a defective soil,

should a portion of it be implanted in this region. How far upward from the internal os this shift occurs is a matter of conjecture. How, then, may we explain the bleeding which often occurs in such cases before the onset of labor?

It has long been considered by many authorities that the cervix is not "taken up" in the latter part of pregnancy, before the onset of labor, to become a part of the lower segment. Webster⁷ so states in his textbook, and further adds that, therefore, this has nothing to do with the cause of bleeding before labor in cases of marginal or lateral placenta previa. More recent authors do not discuss the point in detail, simply state that bleeding before labor is caused by the painless contractions of the uterus. This is an insufficient explanation. Such contractions could not well be responsible except so far as they may produce changes in the lower segment and cervix, since otherwise the normally placed placenta would frequently become detached, not only by the painless contractions, but also by the much more violent contractions of labor, events which we know rarely occur. As a matter of fact, we have concrete evidence that the point of view expressed by Webster is incorrect and that alterations in cervix and lower segment often do occur before labor sets in. On vaginal examination at or near term, before the onset of painful contractions, the cervix is found to vary markedly; in some, the canal is intact, the cervix at least 4 to 5 cm. in length and quite tightly closed. In these it is evident that little, if any, change has occurred, the cervix has not become incorporated in the lower segment before the onset of labor. If these women go into labor, and we have often put them in labor by rupturing the membranes, the process is usually a long one, since a variable number of hours (eight to twelve) is occupied in obliterating the canal. Little or no dilatation of the external os occurs until after obliteration has taken place. In such women one would not expect bleeding to occur until the onset of labor even if the placenta were situated low in the uterus. In other women, vaginal examination reveals that the canal has already been obliterated before the onset of painful contractions; the margins are thin, the external os is partially dilated, sometimes 2 to 3 cm. In these women, labor is invariably much shorter in the absence of other complicating conditions. The reason is that much of the work has already been done; when labor pains set in, they result immediately in dilatation. Again this has been confirmed by experiences in inducing labor under such circumstances. In these women, should a placenta previa exist, one would certainly expect bleeding to occur before the onset of labor. Naturally there are all gradations between these two extremes, women in whom more or less obliteration of the canal, or "taking up" of the cervix has occurred before the onset of labor.

These facts allow of no other explanation than that the cervix very often *does* become a part of the lower segment before the onset of labor.

of the internal os before dilatation has been completed, separation and bleeding may not always be produced. On the contrary, in some instances of antepartum bleeding, one may not be able to feel the placental margin, yet actually bleeding may be due to separation of a placenta so low in the lower segment that it has been caused by alterations in the cervix. I am inclined to think that this happens often. For these reasons, it is practically impossible to estimate the true frequency of the condition. It may be present anatomically, but not manifest itself clinically; it may cause bleeding, yet be diagnosed premature separation of a normally implanted placenta. These facts must be borne in mind in considering any statistical study of these two conditions; we may make very erroneous deductions as to morbidity, mortality and the like.

Indeed, in an attempt to study statistically the 127 cases of antepartum bleeding, not definitely due to some cause (such as cervical erosion) other than placental separation, which occurred in this Clinic in the fifteen-year period 1920 to 1935, I was unable to divide them definitely into cases of placenta previa and premature separation of the normally implanted placenta. It was necessary to group them as cases of definite placenta previa, demonstrated by vaginal examination and the subsequently revealed pathology (35 cases); definite premature separation as demonstrated by the absence of previa on vaginal examination, and the presence of a depressed area on the placenta (28 cases); presumable premature separation, previa being ruled out by vaginal examination, yet placental pathology being absent and hemorrhage slight (33 cases); and finally a group of frankly unexplained cases—unexplained because bleeding was slight, the patients were not examined vaginally, merely treated expectantly, with the result that bleeding ceased, uncomplicated delivery occurred, and the placenta failed to show evidences of premature separation of any type (31 cases). Therefore it seems to me impossible to consider these two conditions apart, except for the extremes, in which we have either the placenta quite patently covering the internal os, or the Couvelaire type of separation.

Concerning the production of bleeding: it is clear that if the placenta actually covers the internal os, or a part of it, as the opening becomes enlarged or retracted the attachments of the placenta are bound to be torn through, and bleeding occur. Should the placental margin merely approach the internal os, the mechanism by which bleeding is produced is not so clear. The mechanism is intimately bound up with the dilatation of the cervix and the formation of the lower uterine segment. As that portion of the cervix above the external os becomes pulled up to become incorporated in the lower portion of the uterine wall, it seems rather obvious on contemplation of the relations as illustrated in Fig. 1, that there is bound to be a shift in the layers composing the wall in this area which would often be sufficient to cause detachment of the placenta

surgeons are much too inclined to use favorite methods routinely. Most gynecologists have been intensely critical of this attitude and emphasize the necessity for classification of the pathology and individual adaption based on sound reasoning before deciding on the choice of procedure to be followed. Such judgment depends for the most part upon a knowledge of normal anatomic relations of the pelvic adnexa and their complete restitution, rather than any ability to diagnose obvious malposition of the uterus.

In deciding upon the method of suspension to be used in the young or middle-aged individual, there are three well-accepted criteria. First, the resulting correction must equal normal position and be permanent. Second, there should be no danger of bowel becoming interposed. Third, under stress of childbearing, there should be no interference with the development of the uterus during pregnancy or dystocia with the onset of labor. In satisfying these requirements, some type of fixation of the round ligaments with or without intraperitoneal shortening seems to have the approval of the majority of surgeons. In the author's experience, either the Olshausen or the Simpson-Crossen modifications of the Gilliam operation with shortening of the uterosacral ligaments presents a means of holding the uterus in normal anatomic position without distortion of the adnexa and the above-mentioned complications are certainly remote.

As the basic technic of these procedures is familiar, the various minor modifications will be eliminated in this paper in order to avoid much sameness. Therefore, standard technic is referred to in the following description.

The Olshausen operation provides for a firm intraperitoneal fixation of the round ligaments against the peritoneum of the anterior abdominal wall by means of sutures which pass deeply into the fascial and muscular layers. Silk, linen, kangaroo tendon, and even silkworm gut have been used in order to obtain a firm fixation and in the majority of cases have proved satisfactory. Such nonabsorbable materials usually remain intact through fibrous inclusion, but in the occasional patient infection invades and the result is nothing short of discouraging. Although direct communication of the infection to peritoneum through the suture canals is a rare happening, nevertheless when it does occur the surgeon is thereafter willing to place his trust in catgut exclusively. It is especially characteristic of nonabsorbable materials to delay the immediate formation of early fibrinous adhesions which are so necessary to seal the suture canals. Consequently, in the presence of an early virulent infection there is always danger of peritonitis. Catgut, on the other hand, is likely to undergo absorption in the presence of either early or late infection with weakening of the points of fixation. Actual rupture, with either one-sided torsion or a return of the uterus to retroposition.

Further I believe that this offers a reasonable explanation for the production of antepartum bleeding due to placenta previa, both before labor sets in and after. That it might not be the sole cause is readily admitted.

One further observation in this specimen is of interest. It will be seen in Fig. 1 that there is a large circular sinus encircling the cervix at the level of the internal os. This sinus is probably that which is found dividing the upper and lower segments late in labor. The observation suggests that only the cervix enters into the formation of the lower uterine segment. Bandl's explanation is not generally accepted today, nevertheless I feel that the matter is not a settled one. Certainly the presence of decidua below the retraction ring cannot be regarded as proof of the double origin of the lower segment, for one may find decidua even well down in the cervical canal as illustrated in this case.

SUMMARY

An anatomic description of a case of marginal placenta previa is presented. Interesting findings were: marked scarcity of decidua beneath the placenta, relatively profuse decidual reaction in the cervix and lower uterus, and presence of a circular sinus at the level of the internal os. The implications of these findings regarding etiology, frequency, the cause of bleeding, and the lower uterine segment are discussed.

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VENTROSUSPENSION OF THE UTERUS WITH LIVING SUTURES

A PRELIMINARY REPORT

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ALTHOUGH nonoperative treatment of retroversion of the uterus is the method of choice in appropriate cases, there is still that large group in which only surgical means of correction can ever bring dependable help. Intraperitoneal operations for mechanical suspension of the uterus by means of utilizing the round ligaments are so numerous, that a balanced consideration of the subject and final conclusions are nearly impossible. It is fair to state, however, that because of familiarity with technic and a satisfactory degree of success in a large series of cases

reflected upward, exposing a large area of both rectus sheaths. The skin and fat apron is then retracted forcibly upward. Starting as high as possible at the lateral border of the recti muscles on each side, two strips of full thickness fascia approximately $\frac{3}{8}$ of an inch wide and 3 inches long are cut from above downward following the outer border of the muscle. This will result in a slight convergence of the strips inward at the pubis as the muscle borders curve inward at this point (Fig. 1). This leaves a narrow point of attachment of the fascia to the pubis in the interspace between the strips. The fascia is here cut across transversely (indicated by dotted line Fig. 1) and the middle fascial apron is reflected off the muscles upward completely denuding the lower central area.

The recti muscles are then separated in the midline in the usual manner and the peritoneal cavity entered. With wide retraction this incision allows adequate exposure of the pelvic adnexa for any additional surgical treatment.

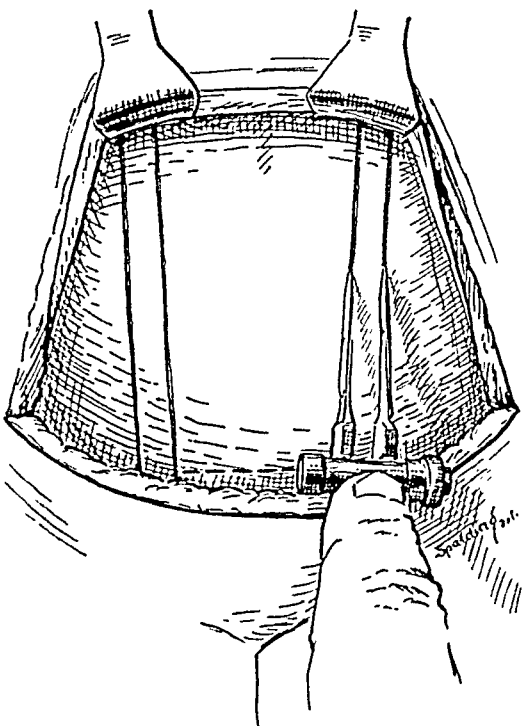


Fig. 1.

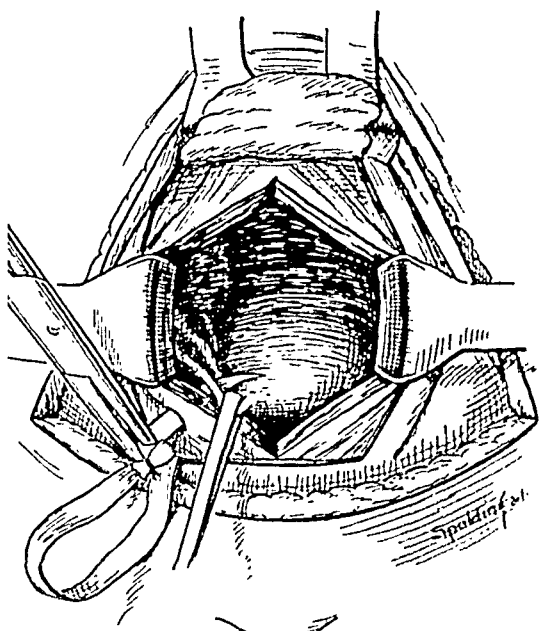


Fig. 2.

Fig. 1.—High retraction exposes large area of rectus sheath. Full thickness strips of fascia cut from above downward following outer border of muscle. Transverse dotted line represents location where fascial apron is cut across in order that it may be reflected upward.

Fig. 2.—Fascial strip has been detached above but left attached below and free end threaded into fascia needle. Needle is carried through abdominal parietes and round ligament is picked up in the usual manner. Strip on opposite side remains in situ until needed for use.

The uterus is then drawn up from the retroposition and the round ligaments grasped one inch from the uterine attachments by means of Allis forceps and held taut. The previously prepared fascial strip on one side is then severed at its upper attachment and with a few sweeping strokes of the knife is dissected off the muscle down to the pubic end where it is left attached. The free end is threaded into a special fascia needle, overlapped upon itself and tied securely with linen (Gallie method).

The needle is then passed through the midportion of the muscle at the desired level perforating the underlying peritoneum to enter the abdominal cavity, when the strip of fascia is drawn through. The round ligament is then picked up beneath

then occurs and further chronic invalidism of a worse sort results. Such accidents invariably bring condemnation to a favorite suture material, and then begins the usual search for something better.

The Gilliam operation including various modifications is somewhat different with respect to dangers from infection or rupture of sutures in that the ligaments are drawn through the abdominal wall and fixed extraperitoneally in the parietes. Formation of early fibrinous adhesions between the coapted tissues is therefore immediate and assured as conditions are more strictly histologic. Moreover the ultimate fate of the suture whether nonabsorbable material or catgut is not nearly so important as it is extraperitoneal. Peritonitis is virtually impossible and the worst that can happen is an encysted abscess around the suture with sloughing and discharge of the suture from the wound. The latter has been so common with nonabsorbable materials in both the Olshausen or Gilliam operations that forty-day chromic catgut is now almost universally employed. Foreign body irritation does predispose to infection, and therefore it is reasonable to assume that in the so-called clean cases a mild degree of infection always exists but disappears through resolution and never becomes evident.

In reviewing the literature on uterine suspension, one finds that the matter of correct methods of suturing the round ligaments and the relative merits of the materials to be used are given great attention. This would indicate that any of the materials thus far tried have given some degree of satisfaction, but still leave something to be desired. Having had a proportionate share of disappointing cases due to rupture of sutures and to sepsis, the author became interested in the possibility of using living fixation sutures to substitute for older methods. The results obtained with living sutures have been sufficiently gratifying to risk a somewhat premature report of a small series of cases.

Strips of fascia from the anterior rectus sheath $\frac{3}{8}$ of an inch wide have been used rather than fascia lata both because of ease of handling and avoidance of unsightly thigh scar. That fascia as suture material becomes permanently imbedded, is unyielding and readily invests itself into fibromuscular structures is now an established fact and therefore should be ideal suture material for this purpose.

Both the standard Olshausen and Gilliam types of round ligament fixation have been tried with minor variations only in the cutting and handling of the suture itself. Many such variations are, of course, possible. The following method to be described has been used in the author's patients so far done.

OPERATION (OLSHAUSEN) WITH FASCIAL SUTURES

The skin and fat layers of the abdomen are incised through a Pfannenstiel incision down to the fascial sheaths of both recti muscles. These layers are grasped together and by means of gauze dissection and sweeping strokes of the knife are

OPERATION (GILLIAM) WITH FASCIAL SUTURES

The Gilliam method needs no extended technical description. Incisional approach is the same as above (Pfannenstiel) with preparation of the strips identical. The uterus is drawn up into correct position by means of drawing the round ligaments through the abdominal wall for extraperitoneal fixation. The actual use of fascial suture consists in merely picking up the loop of ligament where it comes through above the outer border of the rectus muscle and anchoring the free end through itself at its pubic attachment (Gallie method).

The ligament in this case is held by a loop of fascia, the anchorage of which is at the firm pubic attachment and for purposes of description can be likened to the links of a chain. This living suture eventually forms an extraperitoneal, tendinous, accessory ligament. Here, caution must be used not to leave the fascial loop too long as the round ligament may then recede into the abdomen and allow the uterus to hang loosely. In the few Gilliam type operations that have so far been

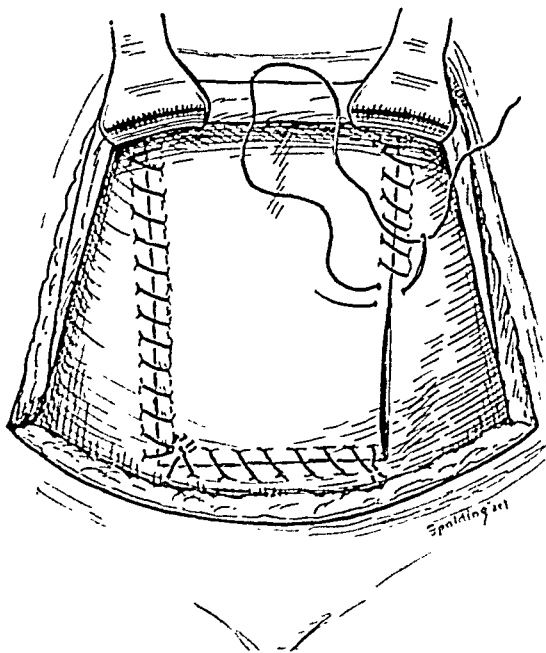


Fig. 5.—Peritoneum has been closed, fascial apron replaced over muscles and sutured transversely to its pubic attachment. Lateral leaves of fascia closed with running suture approximating muscles.

done, it has seemed advisable to pull taut on the suture until the round ligament just barely appears at a level with the anterior surface at the outer border of the rectus muscle. This will approximate the uterus to the abdominal wall correctly.

PRELIMINARY REPORT OF CASES

In all, 27 patients ranging in age from twenty-three to forty-one years have been operated upon and had the Olshausen type round ligament fixation done with fascial sutures. Four were done for virginal retroversion uteri and 23 for varying degrees of procidentia in which vaginal plastic repair of one type or another was combined. Pregnancy has intervened in one of the virginal cases and 5 procidentias. These six patients went to term with no untoward symptoms during the carrying

the Allis forceps in the usual manner (Fig. 2). The needle is then carried through the abdominal layers again in the reverse manner just medial to and at the same level as the point of entrance. The strip is pulled taut to approximate the ligament to the anterior abdominal wall (Fig. 3). The strip is fixed upon itself near the pubic attachment after the method of Gallie.

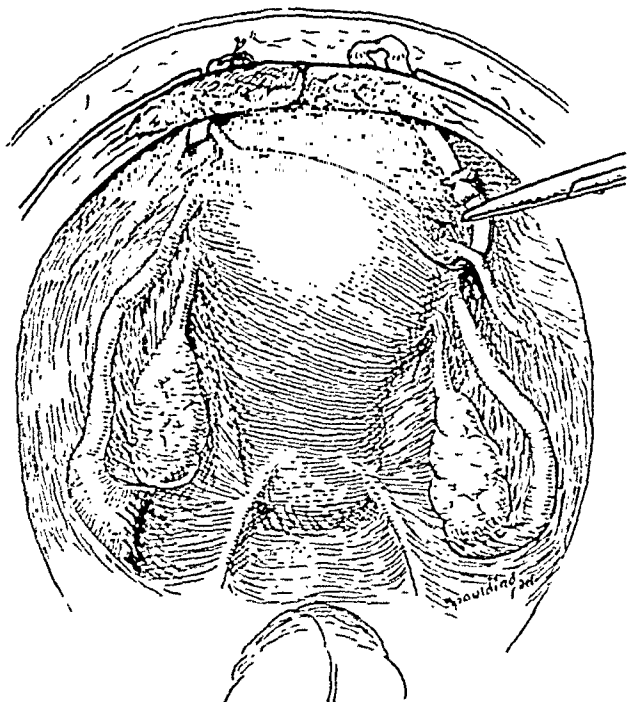


Fig. 3.—Needle and strip have been carried through abdominal parietes in the reverse manner drawing round ligament flush to anterior peritoneum. Strip is fixed upon itself at the pubic attachment. Opposite side illustrates strip being drawn through and round ligament being picked up with fascia needle.

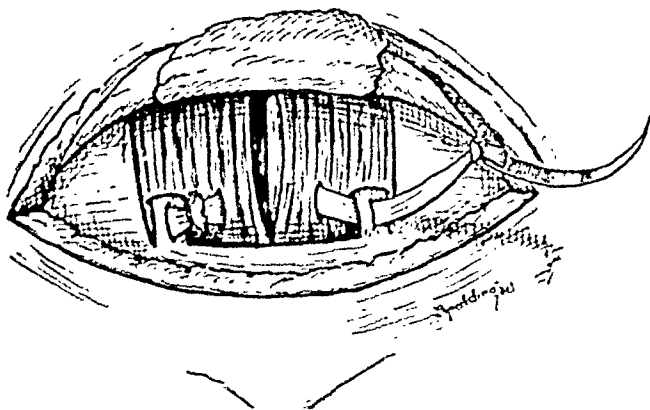


Fig. 4.—Right side anchorage complete. On the left, strip has been drawn through itself in preparation for anchorage (Gallie method).

This maneuver is repeated on the opposite side which completes the operation of Olshausen's round ligament fixation with living sutures (Fig. 4). The peritoneum is closed tightly. The fascial apron is replaced, sutured transversely to its pubic attachment and closed with a running suture on both sides (Fig. 5). The slightly added tension of fascia from approximating the lateral incisions produces excellent coaptation of the recti muscles and thoroughly covers both anchorage points of the fascial suture on the lower anterior muscle.

This operation will be used by me with increasing frequency until a sufficiently large number of cases are collected when a further and more critical report will be made. In the interim, it is recommended as thoroughly safe for gynecologic surgeons to use and a fair trial by other surgeons with evaluation of the results should prove interesting and profitable.

SUMMARY

1. A new technic of performing Olshausen's round ligament ventro-suspension of the uterus through the use of living sutures is presented.
2. A constant large percentage of failures in maintaining position of the uterus together with the frequency of sepsis through the use of foreign suture materials, justifies trial of the method.
3. Later a more complete and critical report of results in a larger series of cases will follow this publication.

45 BAY STATE ROAD

✓A REVIEW OF SEVENTEEN CASES OF INTERESTING ANOMALIES OF THE FEMALE GENITAL TRACT*

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ANY consideration of anomalous structures may well be prefaced by a brief review of the embryology of the system involved. This is done because, as a rule, the cause of the anomaly is not known, and it is necessary to hearken back to the embryologic anlage from whence it arose in order to find the excuse for its existence.

In the 10 mm. embryo a mass of epithelium arises from the celomic epithelium of the lateral surface of the urogenital fold in the region of the third thoracic segment. This mass of cells becomes invaginated and forms a groove; the margins of the lips of this groove fuse at the caudal end to form a tube with an open cranial end. This is the primitive müllerian duct. The caudal end of this tube grows downward along the urogenital fold and as it grows caudad, it crosses the ventral surface of the mesonephritic duct and meets its fellow from the opposite side in the genital cord, and together they pass to the dorsal wall of the urogenital sinus. The adjacent termini fuse during the second month to form a single tube, the uterovaginal primordium, which in the third month opens into the urogenital sinus on a small eminence, Müller's tubercle. The open end of the müllerian duct develops a series of pro-

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period; 5 were observed and delivered personally by the author and one by a hospital interne. Low forceps and episiotomy was the method of completing the second stage in all. None of these patients had difficulty in labor and their postpartum convalescence was normal. Subsequent observation showed involution to be unretarded and that the uterus was maintained in erect position.

It is now over five years since the first patient was operated upon by this method and delivered of a full-term child; recent examination of this patient showed the uterus to be held in erect position, adnexa normal, and she states that her general health has been excellent. There have been no second pregnancies so far in this small series.

As suggested in the above title, this report is distinctly preliminary as definite conclusions are not justified on such a small experience. The operation has only been tried in the occasional selected case in order to ascertain the logic of the mechanics and draw comparisons with a larger experience in orthodox procedures.

COMMENT AND CONCLUSION

It is apparent from the operative description and illustrations that in principle there is practically no variation from the usual Olshausen technic except that the fascial suture is fixed on the anterior surface of the muscle and covered by rectus sheath; it might easily be drawn through the sheath and fixed on the anterior surface in the orthodox manner, but this is obviously unnecessary.

By using living suture a permanent tendinous band is established which invested in peritoneum, muscle, and fascia acts as an accessory ligament. The round ligament instead of being held precariously to a loose and elastic peritoneum by adhesive fixation alone, is anchored permanently to an unyielding abdominal parietes at the desired level. Within a few hours the suture channels are sealed with fibrinous exudate and in seventy-two hours fibroelastic invasion has begun.

Meticulous care should be used in the tying off of all small vessels before closing the sheath of the recti muscles, as a moist wound delays healing of the layers and predisposes to late sepsis. Should there be an uncontrollable capillary bleeding, it is advisable to insert a rubber drain in the midportion of the incision. This drain can usually be removed within forty-eight hours.

Postoperative incisional hernia is as unlikely in this approach to the pelvis as when the classical Pfannenstiel incision is used. Provided there are no postoperative complications and the incision heals by first intention, the hospital convalescence can be held to a maximum of ten days.

The Olshausen method is to be preferred to the Gilliam because of simplicity in technic, lessened painful tension of the round ligaments postoperatively, and a more complete assurance against dystocia.

Kermauner¹⁰ believed that a persistence of the cloaca is an important factor, while Felix⁵ expressed the opinion that formative disturbances of the intestinal tract and developmental errors of the ventral abdominal wall are elements which contribute to uterine abnormalities. The theory of a primary trunk or pelvic defect was supported by Pfannenstiel¹⁸ who said that a primary broader anlage of the lower part of the trunk might cause a failure of union of the müllerian ducts. Variants of this theory are those formulated by R. Meyer¹⁵ and by Kussmaul.¹² R. Meyer maintained that uterine abnormalities are caused by too great a separation of the ilio-inguino-diaphragmatic ligaments or a shortening of the round ligaments which might cause a torsion and separation of the müllerian ducts. Kussmaul expressed the opinion that the persistence of the rectovesical ligament, which is seen in cases of uterus didelphys, keeps the lower ends of these ducts from uniting.

The outstanding champion of the separation of the müllerian ducts by the growth of a tumor is Pick.^{20, 21} He expressed the opinion that stray cells of müllerian tissue or a tumor anlage may keep the ducts apart. C. W. Anderson,² in 1931, put forth a new theory which has certain interesting features. According to his theory, premature fusion of the müllerian ducts results in uterus rudimentaris solidus duplex with absence of the vagina; delayed fusion of these ducts results in uterus unicornis with one rudimentary horn, partial fusion of these ducts results in uterus bicornis with either one or two cervixes, failure of fusion of these ducts results in uterus didelphys, and failure of fusion of the mesenchyme after fusion of the müllerian ducts gives rise to uterus infantilis.

The classification of anomalies of the tubes, uterus, and vagina (Fig. 1) is necessarily as complex as are the theories as to their origin. For simplicity and ease of understanding the schema outlined in Kaufmann's *Spezielle Pathologische Anatomie* is probably the best. A slight modification of this is given in Table I.

TABLE I. UTERINE ANOMALIES

- I. Simple reduplication
 - A. Incomplete joining of Müller's ducts
 1. Symmetrical false reduplication: uterus didelphys
 - B. Complete joining of Müller's ducts
 1. External junction with persistence of the partition: uterus septus duplex
- II. Rudimentary development
 - A. Aplasia
 1. Incomplete development of both sides (symmetrical)
 - a. Absence of tubes, uterus or vagina
 - (1) Absence of uterus
 - (2) Absence of parts of uterus or vagina
 2. Incomplete development of one side (asymmetrical)
 - a. Absence of one side of uterus: uterus unicornis
 - B. Hypoplasia
 1. Symmetrical or asymmetrical development with hypoplasia of one or more parts
- III. Atresia of vagina, cervix, or fundus of uterus

jections, the fimbria. The paired portions of the müllerian ducts form the fallopian tubes. The cranial end of the uterovaginal canal develops into the fundus of the uterus, the middle portion develops into the cervix, and the caudal end becomes the vagina (Jordan and Kindred).⁸

The origin of the lower third of the vagina is a debated question and one that apparently is open to considerable controversy.

Vilas expressed the opinion that the perforation between the sinus urogenitalis and the uterovaginal canal at the müllerian tubercle does not take place. She said that the connection between these two structures is maintained by paired parallel thickenings of the walls of the uterovaginal canal, which she called the "müllerian swellings." The epithelium of the sinus urogenitalis grows between the wolffian ducts and the side walls of the uterovaginal canal and finally fills up the space occupied by the müllerian swellings. This paired proliferation of cells meets in the midline to form an epithelial mass, which Vilas called the "sinus epithelium." At the same time the walls of the uterovaginal canal proliferate anteriorly and posteriorly to form a solid epithelial plate which Vilas called the "müllerian epithelial



Fig. 1.—Anomalies of the tubes, uterus and vagina (after Kaufmann).

plate." Thus, the vaginal anlage consists of two portions, the cranial müllerian epithelial plate and the caudal sinus epithelial plate. At the end of the sixth month, the müllerian epithelial plate cannot be seen, and the vaginal anlage consists entirely of the remaining portion. The cells of this caudal portion become large, pale, and arranged in whorls. The central cells then degenerate and there arises a central cavity which is lined by squamous epithelium.

There are a number of theories as to the origin of uterine abnormalities; perhaps the very number of these theories is sufficient evidence that proof of the genesis of such abnormalities is lacking. The current theories may be roughly grouped to include: (1) antecedent and coincident cloacal and intestinal anomalies, (2) primary anomalies of the trunk or pelvis, (3) tumors, (4) abnormal fusion of the müllerian ducts or failure of absorption of the septum. Among those who considered that the intestinal anomalies were primary was von Winkel,²⁶ who believed that disturbances of development of the intestinal tract, bladder, or a cystic allantois will lead to anomalies of the uterus.

CASE 2.—The patient was an infant, aged three days, who had no siblings. At necropsy a uterus didelphys was found. Other abnormalities included imperforate anus, esophagotracheal fistula, vesicorectal fistula with imperforate vagina (Fig. 3), perforated interventricular septum, accessory suprarenal gland, and accessory pancreas in the stomach.

CASE 3.—A girl, aged four years, had two brothers who were living and well. There was no familial history of congenital abnormalities. A uterus didelphys with septate vagina was disclosed at necropsy. Other abnormalities included separation of the pubic bones, absence of the twelfth ribs, and an accessory muscle band in the right ventricle.

External Junction With Persistence of Septum (Group I B 1).—CASE 4.—A white woman, aged thirty-nine years, first came to the clinic for resection of a vaginal septum and dilatation and curettage for incomplete abortion. The pregnancy had occurred in the right side of a double uterus. She returned later and died of chronic ulcerative colitis, bronchopneumonia with abscesses and gangrene.

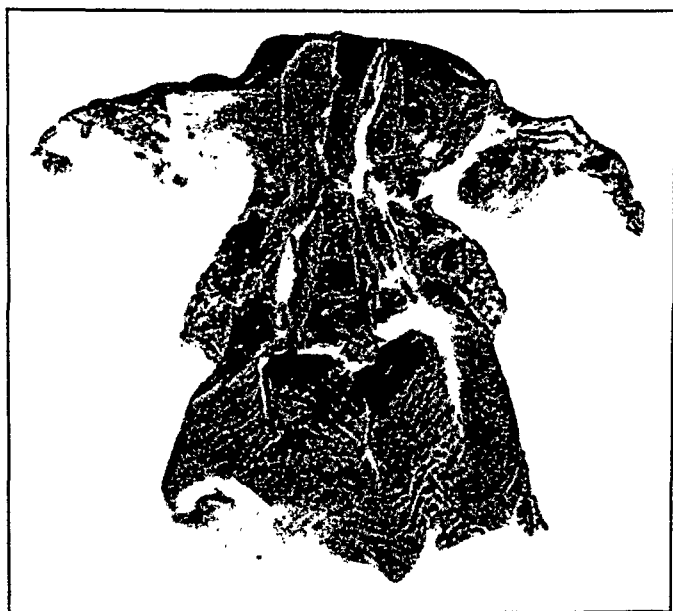


Fig. 4.—Uterus duplex with septate vagina in Case 4; vaginal remnant is represented by the elevation on the posterior vaginal wall.

She had been married thirteen years and had had one pregnancy, the one noted previously. She had one brother and one sister who were living and well. There was no history of familial abnormalities. Her menses had started at the age of thirteen years; had occurred every three or four weeks and had lasted two or three days. Necropsy disclosed a uterus duplex with septate vagina (Fig. 4). A small subserous fibroid also was noted. No other abnormality of a congenital nature was found.

CASE 5.—A white female infant was stillborn. The mother had a uterus bicornis duplex with a vaginal septum. Necropsy revealed that the infant had a uterus duplex with septate vagina. There was no other abnormality of a congenital nature.

CASE 6.—The patient in this case was a white female infant, aged fifteen days. The familial history was not noted. Necropsy revealed an imperforate anus (cloaca) and uterus duplex with septate vagina. In addition, there were hydronephrosis Grade 3 (Fig. 5), spina bifida occulta of the first sacral segment, and a patent ductus arteriosus.

MATERIAL

Material for this study consists of a group of seventeen cases in which the patients came to necropsy. This group includes a wide variety of abnormalities and will be presented roughly in the order noted in Table I.



Fig. 2.—Uterus didelphys in Case 1.

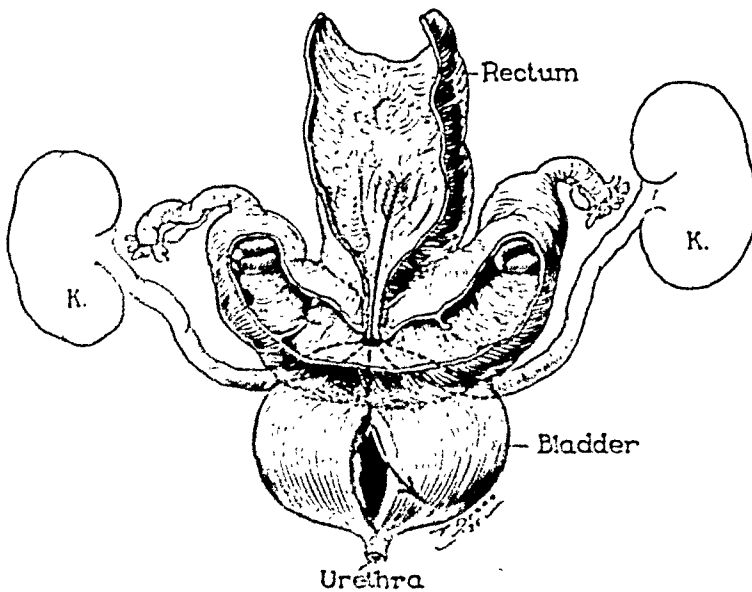


Fig. 3.—Sketch of genitourinary anomalies found in Case 2.

Simple Symmetrical Reduplication (Group I A 1).—CASE 1.—The patient was a married white woman who was forty-four years of age. Her menses had started at the age of fourteen years, had recurred every three weeks and had lasted seven days. She had never had any children. Necropsy revealed a uterus didelphys and a vaginal septum (Fig. 2). No other abnormality was noted.

CASE 7.—A white woman, aged forty-three years, had been married eighteen years but had not become pregnant. Her menses had been normal. Necropsy revealed a uterus subseptus and multiple leiomyomas (Fig. 6). The left fallopian tube and ovary had been removed at a previous operation and the right pelvis was the seat of a tuboovarian abscess. No other congenital abnormality was noted.

Rudimentary Uterus With Absence of Vagina (Group II A 1).—CASE 8.—The patient in this case was a single white woman, aged twenty-eight years. She had one sister who was living and well, but who had one child with spina bifida. The patient's grandmother had had one child who was deformed. The patient had never menstruated. Her breasts and vulva were developed about normally. Necropsy revealed a uterus rudimentaris solidus duplex with artificial vagina. There was also a unilateral ectopic single kidney with fusion at the upper pole; this kidney was situated to the right of the mesospinal line, just above the pelvic brim. There was only one renal pelvis and one ureter; the latter opened into the renal pelvis at the usual site of the left ureteral orifice. No ureteral orifice was noted on the right side.

CASE 9.—A white married woman, aged twenty-two years, had four brothers and two sisters who were living and well. She never had menstruated, but each month she had noted backache, cramps, and weakness. She had been married five years and had carried on intercourse through the urethra. Recently, she had noted nocturia, urinary frequency and burning, and occasional hematuria. Necropsy revealed a uterus rudimentaris solidus duplex. There was a polyp of the bladder at the urachal opening and a diverticulosis of the colon.

CASE 10.—A white woman, aged twenty-four years, had one brother and one sister, who were living and well. She had never menstruated, but monthly had noted some cramps in the lower part of the abdomen. The vagina was about 1 inch (2.5 cm.) in length and the urethra was dilated and ragged. There was some urinary incontinence. The patient had been married three years. Necropsy revealed a uterus rudimentaris solidus duplex with an artificial vagina (Baldwin type).

Rudimentary Uterus With Incomplete Development of One Side (Group II A 2).—CASE 11.—A white woman, aged thirty-three years, had two brothers and three sisters who were living and well. She had been married twice; with her first husband she had had four children, all living and well, and one stillbirth. She had noted some menorrhagia for eight days before she came to the clinic, but for two years prior to her death the menses had lasted four to five days. Necropsy revealed that the fallopian tube, ovary, kidney, ureter, suprarenal glands, and renal artery were absent on the right side. There was a dimple in the bladder at the site of the right ureteral orifice, and there also was a dimple in the aorta at the site of the right renal artery. The left kidney showed a compensatory hypertrophy and weighed 310 gm.

CASE 12.—A single white girl, aged sixteen years, had one brother and one sister who were living and well. Her menses had started at the age of thirteen years, had recurred every three weeks, and had lasted seven days each time. She had not experienced any difficulty during menstruation. Necropsy revealed an absence of the tube and ovary on the left side and a hematoma of the right ovary.

CASE 13.—The parents of a stillborn female infant did not give any familial history of congenital abnormalities. Necropsy on the infant disclosed a single uterus on the left side; the left tube was situated in the normal position and the left ovary was situated near the horn of the uterus. The left tube ended blindly at a point near the lower part of the uterus. The left ovary consisted of an elongated, thin structure which was situated close to the tube throughout its length. Other abnormalities noted included a meningomyelocele with internal hydrocephalus (Grade 2

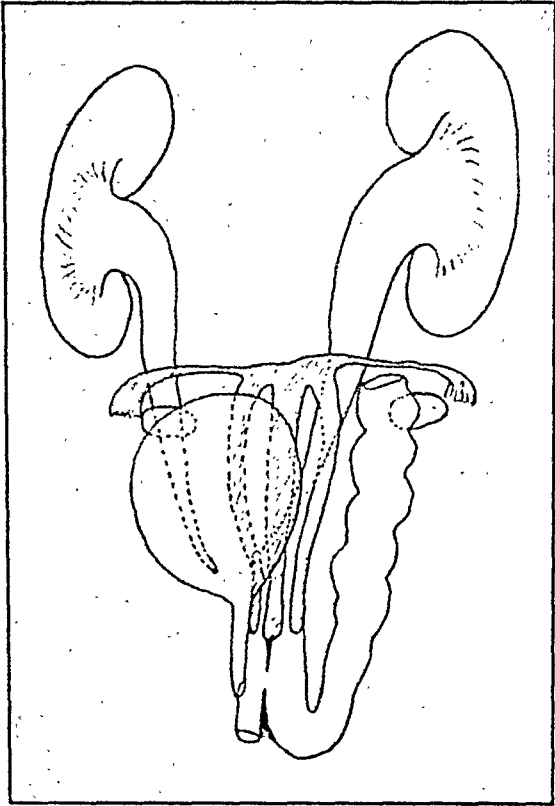
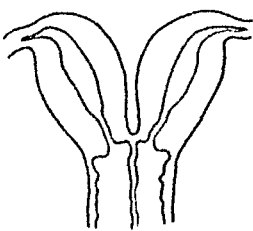
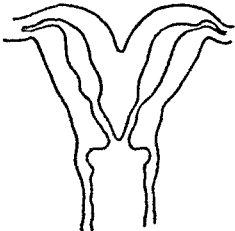


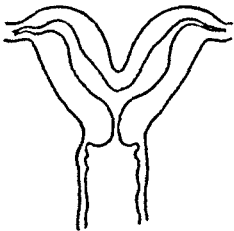
Fig. 5.—Anomalies noted in Case 6.



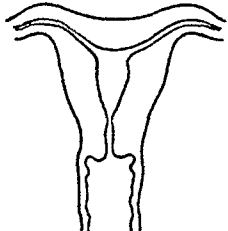
Uterus didelphys



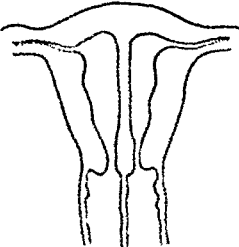
Uterus bicornis duplex



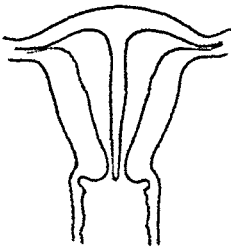
Uterus bicornis unicollis



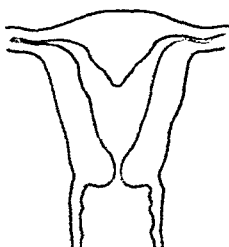
Uterus arcuatus



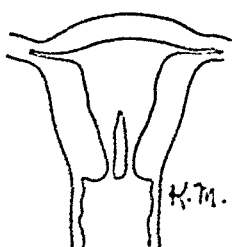
Uterus septus duplex et vagina



Uterus septus duplex



Uterus subseptus



Uterus biforis

Fig. 6.—Uterus subseptus in Case 7.

COMMENT

The frequency of uterine abnormalities has been variously estimated. Smith,²² in a résumé of the cases reported from the New York Lying-In Hospital, said that the incidence of uterine abnormalities among pregnant women was 1 in 1,458. The most frequently encountered abnormality in his series of 35 cases was uterus duplex with septate vagina. There were 12 such cases in his series. Findley,⁶ in his paper on uterus didelphys, said that Stolper²⁴ noted 10 instances of uterus didelphys among 7,400 married women and that Neugebauer¹⁷ noted 3 instances in 19,000 examinations. Haynes⁷ found 6 instances of bicornate uterus, 1 instance of uterus septus, and 4 instances of uterus didelphys in the 11 cases he reviewed.

In the 17 cases which form the basis of this report, the incidence of congenital anomalies of the female genital tract was as follows: uterus didelphys, 3 cases; uterus duplex and septate vagina, 4 cases; uterus rudimentaris solidus duplex with absence of vagina, 3 cases; absence of fallopian tube and ovary, 2 cases, and uterus unicornis, abnormal insertion of fallopian tubes, hemihypoplasia of uterus, rudimentary uterus with atresia of the vagina, and atresia of a fallopian tube, 1 case each.

Failure of fusion of the müllerian ducts probably represents the most primitive form of anomaly of the female genital tract. The anomaly may be of two types: in one type there is a symmetrical reduplication as represented by uterus didelphys, and in the second type there is an external fusion with incomplete disappearance of the septum, as represented by uterus duplex and septate vagina.

In 3 of the 7 cases in which the genital anomalies were the result of failure of fusion of the müllerian ducts, the patients were married women. Only 1 of these 3 women had ever been pregnant, and in this case the pregnancy had terminated in an abortion. It is interesting to note that these 3 patients did not have any other congenital anomaly or any evidence of dysmenorrhea; however, 1 of these patients had multiple leiomyomas.

A review of the literature indicates that most patients who have uterine abnormalities lead a perfectly normal existence. The abnormality usually is noted by the physician at the time of pregnancy or at pelvic examination in the course of disease of the genital organs or in the presence of entirely irrelevant symptoms which necessitate a complete physical examination. Occasionally one horn of an abnormal uterus may become filled with retained menstrual products and give rise to a unilateral dysmenorrhea. This symptom was first noted by M. H. Phillips.¹⁰ Masson and Mueller¹⁴ as well as D. A. MacDonald¹³ have reported cases of this type.

In considering the means of diagnosis, if the history is unavailing, palpation may often give a clue. Roentgenographic examination following the injection of iodized oil into the uterine horns has been utilized by

on a basis of 4), bilateral talipes equinovarus, an absence of the left kidney (the right was U-shaped) and an absence of the right patella.

CASE 14.—A married woman, aged thirty-three years, had had six children, three of whom were living and well. There were three siblings who were living and well. Her menses, which had started at the age of thirteen years, had been regular and accompanied by a slight dysmenorrhea. Necropsy revealed that the right tube was inserted slightly to the right of the uterine fundus and that the left tube was inserted low on the left side of the uterus near the junction of the cervix and fundus. There also was a congenital absence of the left kidney and ureter.

Rudimentary Development With Hypoplasia of One or More Parts (Group II B 1).

—CASE 15.—A white woman, aged fifty-six years, had been married twenty-five years but never had been pregnant. Her menses, which had started at the age of fourteen years, had been regular and apparently had been without symptoms.



Fig. 7.—Specimen obtained in Case 16; *a*, atresia of vagina (probe indicates vaginal orifice); *b*, rudimentary uterus.

Necropsy revealed a definite hypoplasia of the right half of the uterus and almost complete obliteration of the uterine canal. There was no other congenital abnormality.

Atresia (Group III).—CASE 16.—A girl, aged four years, had three siblings, who were living and well. The patient had been born with a mass on the lower part of the abdominal wall; urine had dribbled from this mass. Necropsy revealed a rudimentary uterus with marked atresia of the vaginal orifice (Fig. 7). Exstrophy of the bladder and separation of the symphysis pubis were also noted.

CASE 17.—A woman, aged thirty-eight years, had two siblings, who were living and well. The patient had had three pregnancies: one child was living and well and the other two pregnancies had terminated as miscarriages. Her menses had started at the age of seventeen years, had recurred every four weeks, and had lasted three days. There was no history of dysmenorrhea. Necropsy revealed an atresia of the left fallopian tube near its junction with the uterine fundus. There was no other congenital abnormality.

finding seems to indicate that there is a distinct possibility of superfetation in cases of double uteri. In the 3 cases of uterus rudimentaris solidus duplex, 2 of the patients had symptoms which were suggestive of menstruation. One of the 2 married women who had this type of genital anomaly gave a definite history of intercourse through the urethra, while the urethra of the other woman was dilated and had a ragged border. In 1 of these cases there was a history of other abnormalities in the family. Of the 4 adult patients who had vaginae and uteri, 1 had menorrhagia, 1 had slight dysmenorrhea, and the other 2 had normal menses. In 5 of the entire group who had genital anomalies which were the result of rudimentary development, other congenital anomalies were present.

The genital abnormality was the result of atresia in 2 cases. There was no family history of congenital abnormalities in either case. In 1 case the patient was a girl, in the other case the patient was a woman who had been pregnant three times. One of these pregnancies had produced a living child but the other 2 had terminated as miscarriages.

SUMMARY

This report consists in a review of the embryology of the female genital system, a brief review of the various theories concerning the etiology of uterine abnormalities, and the pertinent findings in 17 cases of uterine abnormalities. This group represents 11 adults and 6 children. In 2 cases there was a familial history of congenital abnormalities and in 9 cases there were abnormalities other than those of the genital system. Four of the patients had menstrual symptoms and 9 of the patients were married. Five of the married patients never had been pregnant. Four of the patients collectively had been pregnant 15 times. These pregnancies had resulted in 11 children, 1 stillbirth, and 3 miscarriages.

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Steinharter and Brown.²³ These authors, however, specify that the injection of iodized oil for diagnosis during pregnancy should be reserved for those patients in whom continuation of pregnancy is contraindicated.

In the other 4 cases in which congenital anomalies were the result of failure of fusion of Müller's ducts, the patients were infants. Three of these infants also had other congenital anomalies. The mother of the fourth infant had a uterus bicornis duplex with septate vagina.

All types of pathologic lesions may be associated with congenital abnormalities of the uterus. Abramson¹ noted pregnancy in one uterus and fibroids in the other uterus in a case of uterus didelphys. Epstein and Goldberg⁴ reported a case in which a pregnancy in a uterus didelphys resulted in streptococcic peritonitis.

In 8 cases the genital anomaly was the result of rudimentary development. In 7 of these cases the patients were adults and in the other case the individual was a stillborn infant. Five of the women were married and 2 were single. Two of the married women could not have become pregnant because of absence of the vagina. Two of the 3 remaining married women had become pregnant; 1 of these women had had 6 children while the other woman had had 4 children and 1 stillbirth.

The question of fertility in cases of genital abnormalities has been raised many times in the literature. Many authors appear to believe that a patient who has a uterine abnormality is almost certain to be sterile, yet a brief review of the literature reveals that most abnormalities of the female genitalia have been first noted during pregnancy and that many of these patients had had previous pregnancies which apparently had been normal.

Findley reviewed a series of 135 cases of uterus didelphys in which pregnancy had occurred. In these cases, there were 217 full-term babies, 13 twin pregnancies, 15 premature deliveries, and 86 abortions. Malformation of the baby occurred in 2 cases. Dannreuther³ reported 13 cases of congenital anomalies of the female pelvic organs. Eleven of the patients in these cases were married, but 5 of the 11 never had become pregnant. The other 6 women collectively had had 16 children and 11 miscarriages; 5 of the miscarriages admittedly were induced abortions. Smith said that patients who have double uteri show less tendency to become pregnant than do normal women, but that after women who have double uteri once become pregnant, they have the same tendency to become pregnant as do normal women. Smith also noted an increased tendency to abortion and premature labor, and he and Findley both stressed the frequency of abnormal position of the fetus in cases of uterus didelphys. Findley noted 13 breech presentations, while Smith concluded that there was an increase in the incidence of breech and transverse positions in such cases.

In a case of uterus duplex bicornis, Moench found a seven months' fetus in one horn and a three months' fetus in the other horn. This

mate truly representative results. For this reason the literature of the world for the years of 1924 to 1933 inclusive was completely reviewed, and this ten-year period used as a basis. Further than this a second series of unreported cases embracing the same time period was collected. In the actual assembling of the statistics from the literature, papers were studied which were included in the indices under the general heading of placenta previa; probably a number of other cases reported under the headings of cesarean section, version, etc., were overlooked. As will be seen figures presented are from most of the principal countries of the world.

It is no part of the scope of this paper to present a monograph on placenta previa. Such questions as the etiology, the symptomatology, and the diagnosis are left untouched. The object is rather to present the results, in terms of maternal and fetal mortality, of various forms of treatment. Moreover, in this paper, all vaginal forms of delivery are grouped together whether they be spontaneous or by any means whatsoever as "delivery from below," the only stipulation being that the delivery be a vaginal one. This method of delivery is then contrasted with abdominal delivery and the results expressed in various charts and tables.

It should be understood that this study does not necessarily represent a personal view. The method of preparing the data was to collect all cases of placenta previa, noting how they were delivered, and then ascertaining how many women lived and how many died. These, with similar notations as to the infant, were the only criteria employed.

Twenty-two thousand one hundred and fifteen comprise the total number of cases upon which this study is based. Five hundred and ninety-one of these are heretofore unpublished, but were included in the paper through the courtesy of the heads of various clinics in this country and abroad. Unfortunately not all of the published reports contain full information about each and every factor with which the study is concerned; thus, in some parity is not given, in others the degree of placenta previa is not stated. As a consequence some of the charts which follow employ percentage basis thus utilizing all cases in which full data are available.

Chart 1 illustrates the distribution of cases as regards the degree of placenta previa and the parity of the patient. Here a word as to definition is required. The classification used in this study is as follows: if the placenta practically covers the internal os, it is called central; if the os is but partially covered, it is called lateral; if only a margin of placenta is felt, then it is classified as marginal placenta previa. Using these criteria 29.3 per cent were central, 23.6 per cent were lateral, and 47.3 per cent were marginal. In approximately 75 per cent of the series the patient was a multipara, while in 25 per cent she was primiparous. This ratio is higher as regards the primiparas than is usually encountered, but it is thought that authors have tended to report their primiparous cases more readily, as they are frequently more serious and more difficult to handle.

A STATISTICAL STUDY OF THE TREATMENT OF PLACENTA PREVIA*

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OF RECENT years there has been a sharp controversy as to the proper treatment of placenta previa. In general there are three points of view: the radical, so called, favoring cesarean section; the conservative, favoring delivery from below; and what one might call the individualistic, favoring whatever method of delivery seems best in each case. As a consequence there is no established treatment for placenta previa either in this country or abroad.

There are many reasons for this difference of opinion. There are innumerable factors to be considered. It is not necessary to mention all of these, but a few of the more important refer to the type of placenta previa, the parity of the patient, the presentation, the general physical condition, the amount of hemorrhage, the period of gestation, and the equipment available. There are many others. Again the operation of cesarean section was not formerly as safe for the mother as it is today. With the new type of operation women may be cesareanized after they are potentially infected; this was not deemed advisable in former years. Still another reason is the influence of obstetric leaders and teachers and a more surgically minded point of view, at least in this country.

If placenta previa were a frequent complication of pregnancy, obstetric opinion as to its treatment would undoubtedly be more united. The incidence is variously stated, but probably approaches one case in each thousand deliveries. It is more common in hospital statistics for obvious reasons. Therefore any one operator is not likely to see a very large series in a lifetime.

At present most obstetricians seem to be in accord that primiparas with central placenta previa should be delivered abdominally. Conversely, it would appear that the multiparous woman with a marginal previa, well advanced in labor, should be delivered vaginally. Between these two extremes lies the majority of cases, and the question of proper procedure in such instances has created a complex situation.

It was felt that a large series collected from the world literature might be of interest. There is little or no use in attempting to draw conclusions from a few thousand cases, as the individual equation of the writer must introduce a factor of error. However, if the series is large enough, the personal point of view tends to be minimized and one should approxi-

*Read before the Section on Obstetrics and Gynecology of the New York Academy of Medicine, May 26, 1926.

truly appreciated. Chart 3 illustrates the maternal mortality by years. Here it is seen that there has been a gradual reduction in mortality regardless of the method of delivery. The chart shows that the mortality from delivery through the vagina was higher in most years than after cesarean section. In only one year, 1932, when there was an unusually high percentage of cesarean sections done, was the mortality rate from this operation relatively high as compared with vaginal delivery.

Chart 4 presents a graph which shows the fetal mortality after various methods of delivery. This is definitely lower, as might be expected, each year with abdominal delivery. Fetal mortality is understood to be a total figure representing stillbirths,

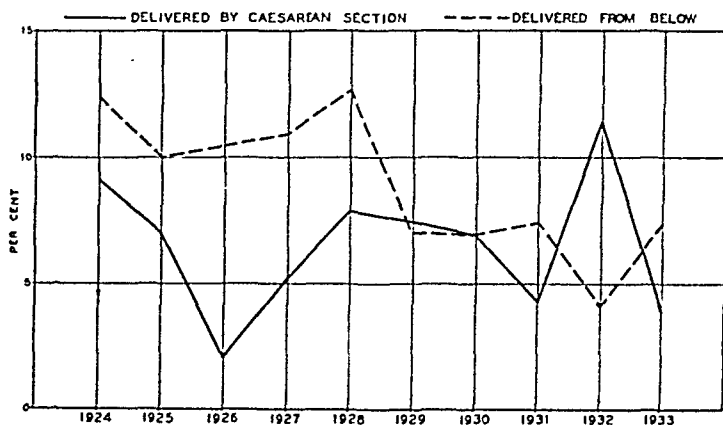


Chart 3.—Maternal mortality in cases of placenta previa delivered by cesarean section and from below (1924-1933).

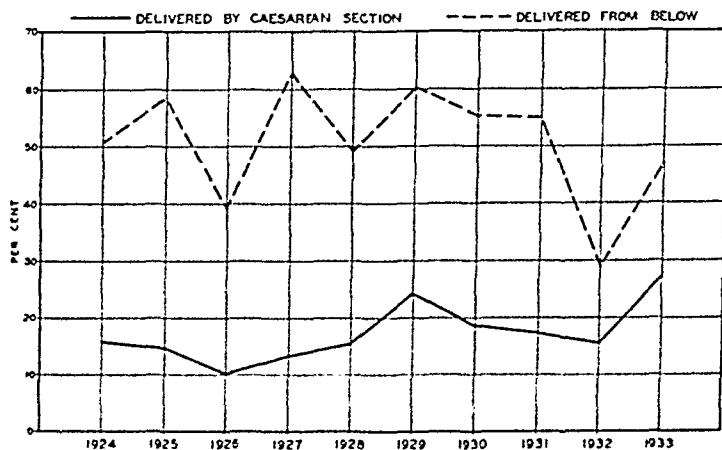


Chart 4.—Fetal mortality in cases of placenta previa delivered by cesarean section and from below (1924-1933).

neonatal deaths, monsters, and immature, nonviable fetuses. Prematurity and immaturity contribute to cause a high mortality rate in any study of placenta previa. In a series as large as this it was felt that any correction which might be made on total fetal mortality would be useless as the various factors would tend to equalize themselves in the contrast between methods of delivery. Total figures show that 17 per cent of the babies born after cesarean section were lost, while 53.7 per cent died following delivery from below.

The treatment and the results of treatment based on the degree of placenta previa existing are presented in Chart 5. As has been stated above, not all the reports provide information as to this factor so this is prepared on a percentage basis, em-

The incidence of cesarean section is demonstrated in Chart 2. One-fifth (19.7 per cent) of the total series was delivered by abdominal section, leaving about four-fifths to be delivered from below. This incidence is divided into years and expressed graphically. Here it is seen that if the high peak of 1927 be disregarded as an artifact there is a more or less regular curve which reaches its peak in 1932. The drop in 1933 is due to the fact that the series for this year is small, as many reports would tend to appear during the year 1934, covering the preceding year's work, and reports appearing in 1934 were not included in the study. If now two five-year

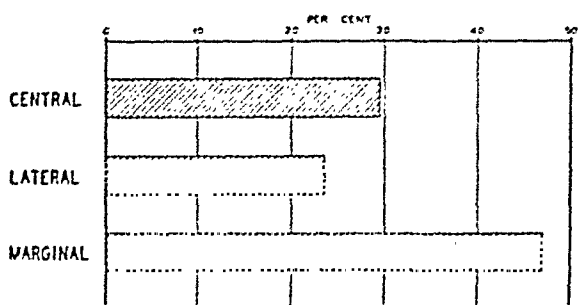


Chart 1-A.—Distribution of degrees of placenta previa.

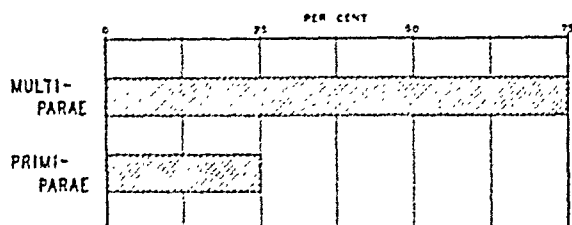


Chart 1-B.—Distribution of primiparas and multiparas.

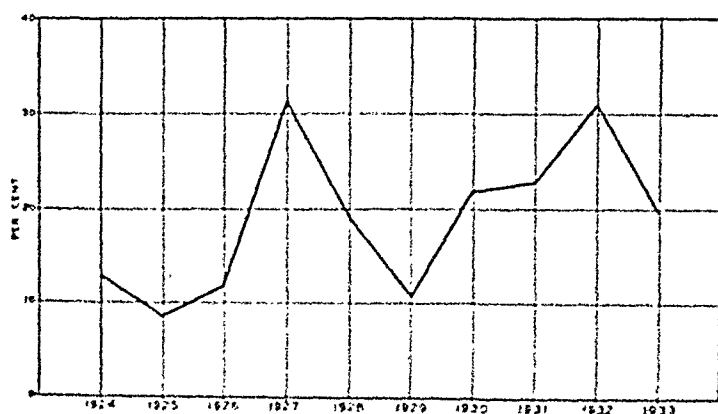


Chart 2.—Percentage of placenta previa delivered by cesarean section (1924-1933).

periods are considered, the incidence of cesarean section from 1924 through 1925 is 16 per cent, while from 1929 through 1933 it is 21 per cent, an increase of 5 per cent. Among other reasons it is believed that this increase may be partly explained by the more frequent and universal use of blood transfusion as well as by the growing tendency frequently to consider placenta previa an indication for surgery.

In the total series the maternal mortality after cesarean section is 6.6 per cent, while after delivery from below it is 8 per cent. In themselves these figures approximate one another, but when it is realized that their numerical expression represents a difference of over three hundred fatal outcomes, their significance is more

per cent for the mother and 65.1 per cent for the baby. In the marginal type of previa less than 1 per cent of the mothers and 28.6 per cent of the infants failed to survive after abdominal delivery, but 6.4 per cent of the mothers and 49.1 per cent of the babies died after delivery through the vagina.

A few rather interesting facts are here brought out. There was almost no maternal mortality in the partial or marginal varieties of placenta previa when patients were cesareanized. The maternal mortality from lateral placenta previa delivered from below is higher than that of central placenta previa delivered by abdominal section. The fetal mortality in partial placenta previa is much higher than that of the marginal type, both types being treated by cesarean section. In each degree of placenta previa, cesarean section gives a lower mortality than does delivery from below.

It should be most clearly understood that these last two charts representing results based on the degree of placenta previa do not include the entire series of 22,000, but only those cases in which full information is specified. However, it would seem to show that the risk of this operation in such cases is not unduly great, although many authorities have held that the opposite is true. It is common practice to consider a placenta previa centralis a more suitable case for section than a previa of one of the other varieties. These studies tend to show that there is a very definite maternal mortality to delivery from below, even in the marginal type. To put it in a more graphic fashion, the mortality in delivery of partial placenta previa from below is more than 3.0 per cent higher than the average mortality of the more than 4,300 cesarean sections performed for all types of placenta previa.

It is of interest to examine the statistics from a geographic point of view. Some countries have been grouped together for this purpose: thus, Central Europe includes Germany, Austria, and Hungary; Great Britain includes England, Scotland, Ireland, Australia, and South Africa; Scandinavia embraces Sweden, Denmark, and Norway; while all of South America is grouped together. The incidence of cesarean section in various countries from which data are available is shown in Table I.

TABLE I

Italy	66.2 per cent
France, Belgium, Netherlands	30.2 per cent
Central Europe	21.4 per cent
Spain and Portugal	20.5 per cent
United States	17.3 per cent
Scandinavia	11.8 per cent
Philippines	8.2 per cent
Russia, Finland, Poland	8.2 per cent
Great Britain	6.8 per cent

This table demonstrates the care which must be exercised in interpreting such statistics as are available. Thus, it is not conceivable that of all cases of placenta previa in Italy, two-thirds of the patients were delivered by cesarean section. However, of the published papers and reports which have been studied, this is a fact. Probably it would be no more than fair to say that there is a distinct tendency toward the so-called radical treatment of placenta previa in Italy. This is reflected in the reports from the Italian provinces in Africa where it may be assumed that the teachings of the Italian schools prevail.

The incidence of cesarean section has been worked out to determine if there has been a trend toward or away from this operation during the past ten years in the various countries. Not all of these nations have reported cases enough each year to make it either accurate or profitable to attempt this study in every instance, so

playing only those cases in which this information is available. Chart 5 shows that cesarean section was performed in 48.3 per cent when the placenta was centrally inserted, in 15.7 per cent when it was lateral, and in 7.5 per cent when it was marginal. The incidence of delivery from below is the reciprocal of these figures.

Chart 6 presents a composite table which shows both maternal and fetal mortality after delivery by cesarean section and from below based on the degree of placenta

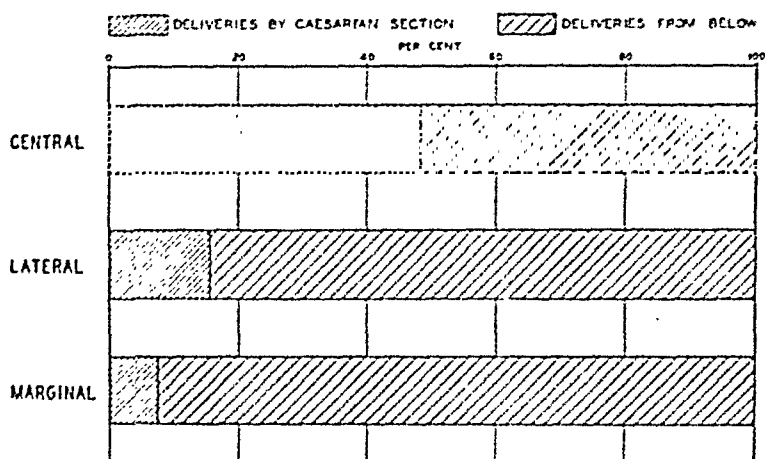


Chart 5.—Percentage of deliveries by cesarean section and from below based on the degree of placenta previa.

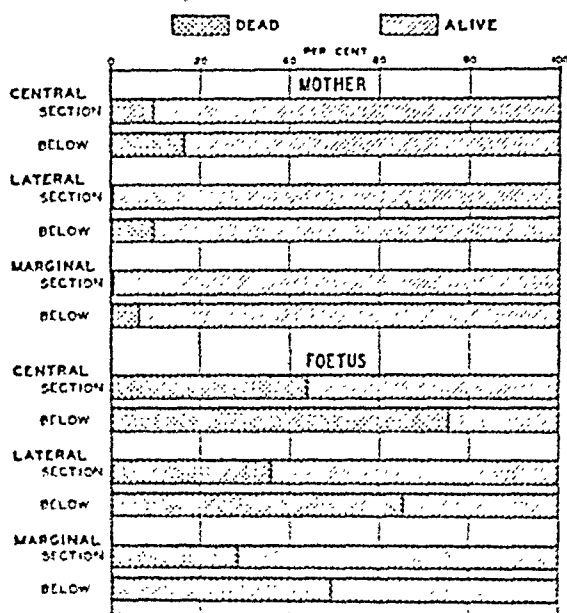


Chart 6.—Percentage of maternal and fetal mortality after delivery by cesarean section and from below based on the degree of placenta previa.

previa. Here again figures are expressed on a percentage basis, and they comprise all the cases in which sufficient data are given. In central degrees of previa when delivery is by abdominal section the maternal mortality is 9.4 per cent and the fetal mortality is 43.7 per cent. After delivery from below these figures rise to 16.5 per cent and 75.0 per cent, respectively. When the placenta is laterally inserted cesarean section provided a death rate to the mother of less than 1 per cent, and a fetal mortality of 15.8 per cent, while other methods of delivery gave figures of 9.7

SUMMARY

A series of 22,115 cases of placenta previa has been studied. This series, the largest noted in the literature, has been taken both from the published reports of the world and from a smaller number of hitherto unreported cases.

The two phases, treatment and the result of treatment, in terms of maternal and fetal mortality, have been considered. Delivery has been divided into two groups: one comprising those women delivered by cesarean section, the other those delivered by any other means. Various other factors such as the parity, and the degree of placenta previa have been studied. Maternal and fetal mortality has also been classified, based according to the degree of previa of the placenta and upon the method of delivery.

In discussing mortality it has been emphasized that total, global mortality is meant. No corrections have been applied in this regard, either in the case of the mother, to those women dying of causes not purely obstetric or, in the case of the baby, to immature, nonviable fetuses, or to monsters.

A study of the trends during the past ten years of the two methods of delivery of this complication of pregnancy has been appended. Further than this, mortality curves for mother and baby have been prepared showing the incidence during the years covered in the review.

Statistics are presented covering the facts reported from the principal countries of the world. Thus the incidence of method of delivery and the results of treatment, again in terms of maternal mortality, are shown, and various contrasts between these factors are drawn.

CONCLUSION

In general, the risk for mother and baby in cases of placenta previa is less when delivery is terminated by cesarean section than it is following delivery from below.

I should like to express my sincere appreciation to Dr. Walter McMann, late of this city, for his very great help in compiling certain of the statistical data which have been used in this study.

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the four principal countries reporting the largest number of cases have been employed to determine this trend. Moreover five-year averages have been given, thus summarizing the incidence from 1924 through 1928, and then from 1929 through 1933. Table II expresses these averages.

TABLE II

	1924-1928	1929-1933
United States	13%	45%
Central Europe	38%	37%
Great Britain	51%	5%
France	92%	23%

It is thus seen that the United States is the only one of these countries in which the trend has been more toward so-called radicalism in the treatment of placenta previa, although the trend in the Central European countries has remained approximately the same. However, when one compares the maternal mortality in the United States during the two five-year periods, it is seen that an increase of 32 per cent in the incidence of abdominal delivery is accompanied by a decrease of about 5.5 per cent in maternal mortality.

The results of treatment of placenta previa in the various countries have been expressed in terms of maternal mortality after delivery by cesarean section and after delivery from below in Table III. The two columns have been arranged to show the countries with the highest mortalities at the top of the list—on the left in terms of patients delivered abdominally, on the right in terms of patients delivered vaginally.

TABLE III

Philippines	21.6%	Russia, Finland, Poland	17.9%
Russia, Finland, Poland	11.1%	Philippines	17.4%
Central Europe	10.2%	United States	10.8%
France, Belgium, Netherlands	7.9%	Great Britain	9.6%
United States	5.9%	France, Belgium, Netherlands	8.6%
Great Britain	5.5%	Central Europe	7.1%
Spain and Portugal	4.7%	Scandinavia	5.8%
Scandinavia	4.6%	Spain, Portugal	4.9%
Italy	0.7%	Italy	4.0%

Or, arranged in a different way (Table IV) with the percentage of maternal mortality after cesarean section and after delivery from below placed after each country.

TABLE IV

Philippines	21.6%	17.4%
Russia, Finland, Poland	11.1%	17.9%
Central Europe	10.2%	7.1%
France, Belgium, Netherlands	7.9%	8.6%
United States	5.9%	10.8%
Great Britain	5.5%	9.6%
Spain, Portugal	4.7%	4.9%
Scandinavia	4.6%	5.8%
Italy	0.7%	4.0%

It is thus seen that some countries, among which are the United States, Great Britain, France, Spain, Italy, and the Scandinavian countries, have obtained better results so far as maternal mortality is concerned by the use of cesarean section. In the other countries, notably in Central Europe, the reverse is true.

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Solomons, Edward, and Dockeray, Gerald C.: Vaginal Discharges, Irish J. M. Sc., page 548, 1936.

Fifty-three women who complained of vaginal discharge and ten normal pregnant women without discharge were examined for *Trichomonas vaginalis*. In a total of 78 cases, 9 had trichomonas present and 8 had *Trichomonas vaginalis* vaginitis. None of the patients without discharge had trichomonas.

The parasite is more frequent in pregnancy and addition of female sex hormone to culture media stimulates its growth (Donne). Unexplained vaginal leucorrhea is often due to this parasite.

At the present time the methods of treatment are numerous and the results vary. The authors employed ichthyol-glycerin tampons with poor results. Devegan gave a better response. The finding of 15 per cent of patients with vaginal discharge containing *Trichomonas vaginalis* warrants the routine examination of all discharges of unknown etiology for the presence of the parasite. In the authors' hands Devegan proved valuable in patients suffering from vaginal discharges due to trichomonas or of obscure origin.

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that radiation has very little effect toward cure. But when the extent of the disease is looked into, we find that practically all patients presenting reasonable hope of cure were subjected to operation, radiation alone being limited to the hopeless cases. Hence, the general results do not show the relative efficacy of radiation even of those days, and much less of the improved radiation of the present.

A uniform method of clinical classification according to extent of involvement is imperative, not only for evaluation of treatment results in reported cases, but also as a guide to the selection of the best treatment for patients as they come day by day. Such classification requires careful examination and accurate recording of findings before operation and then of gross findings at operation and then of gross findings in the laboratory. This division into stages representing extent of growth must of course be founded on a solid pathologic basis. That is, the clinical stages cannot be defined by symptoms but must represent definite extent of growth as determined by examination at operation and in the laboratory. Hence, the stages of the classification to be made before operation as a guide to treatment must be defined in terms of pathologic extent which can be accurately determined only after operation. This paradox shows very well the vicious circle of difficulties encountered, and the reason why the solution of this important problem has been so long delayed.

Having identified the difficulties, we are in a better position to attack the problem successfully. In the first place, it is clear that the stage-classification made before operation cannot be accurate, only approximate. But by utilization of all the factors which help toward accuracy, the preoperative classification may be made to approximate so closely the actual extent as to be of material assistance in the selection of treatment for that patient. The first task is to define the stages in terms of pathologic extent, and the second and more difficult task is to devise a plan of recognizing the stages approximately before operation.

Classification into Stages.—The division of a continuous process into stages necessitates dealing with borderline areas about which there may be differences of opinion as to preferable assignment. However the important thing is not exactly where the lines of division are placed but that they should be placed definitely somewhere, and then that this definite classification be used in all clinical work and in all reports of cases. The following classification into stages is definite and practical, and stands the test of application in the examining room and at the operating table and in the laboratory. Each of these stages was selected with two points in view: first, to have its limits correspond with anatomic lines as far as practicable so as to be well defined and easily described, and, second, to have it recognizable clinically

CLINICAL CLASSIFICATION OF CASES OF CARCINOMA OF CORPUS UTERI*

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THE pathologic grading of carcinomas of the corpus, according to cell type and arrangement, is now on a firm foundation and proving very useful. It helps not only in pathologic study but also in the selection of treatment, especially in the handicapped patient who is near the borderline of operability. This grading by cell type has proved more useful in corpus carcinoma than in carcinoma of the cervix. On the other hand, the attempt at a useful clinical classification of corpus cancer cases has not succeeded as it did with cancer of the cervix, where the clinical classification into stages according to extent of tumor growth is now well established and in general use.

A dependable clinical classification of cases of carcinoma of the corpus is a complicated matter, much more complicated than appears on the surface. It has been delayed by difficulties not found in carcinoma of the cervix. In cervix cancer the location and extent of the infiltration can be determined by direct palpation, and the depth of the vaginal and cervical ulcerations are open to easy and accurate inspection. Not so in corpus cancer, where the various stages of extension into the thick uterine wall defy palpation and inspection, and can be outlined only after the uterus is removed.

However, despite the difficulties, the attempt to work out a satisfactory clinical classification of these cases should be persisted in and vigorously pushed. The reliable and uniform grouping of these cases into clinical stages representing extent of growth is absolutely necessary for the evaluation of treatment results. In comparing the results of different methods of treatment, the comparison must be made between cases of the same approximate extent of involvement, i.e., early cases to early cases, medium advanced to medium advanced, and late cases to late cases. Otherwise there may be erroneous conclusions as to the efficacy of the different treatment methods. This point is illustrated by our Barnes Hospital series of five-year results in corpus carcinoma (*Am. J. Obst. & Gynec.*, 29: 326, 1935). In the fifty-six patients treated before 1929, death resulted in nearly all patients receiving only radiation treatment. Thus the general results would indicate

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ing be due entirely to the carcinoma, its severity is only a very general indication of the extent of tissue involvement, for severe hemorrhage may sometimes come from a small area.

Inquiry is to be made as to previous examinations and treatments. An examination years before may have revealed a fibroid, which fact would account for the enlarged uterus instead of assuming it all to be due to the carcinoma. The patient may have been curetted several months or a year or two previously, and the microscopic report on the curettings may help in closer determination of the beginning of the malignant change.

Pelvic Examination.—Careful bimanual palpation of the pelvic structures is the most useful examination measure in determining the extent of involvement in Stages III to VI inclusive. In Stages I and II hardly any enlargement would be found, except from some complication, and the absence of definite enlargement or induration would narrow the diagnosis to Stages I and II. In a patient with no complicating pelvic inflammation, superficial tenderness of the corpus uteri would indicate peritoneal involvement (Stage III), while deep tenderness only would indicate that the infiltration was still confined to the muscular wall (earlier Stage III or Stage II).

Superficial tenderness about the upper part of the uterus, associated with considerable enlargement and irregularity, should arouse suspicion of involvement of an adherent intestinal coil or area of bladder wall (Stage IV) but does not establish it, for such enlargement and tenderness may be due simply to a projecting mass in the uterine wall with some irritative peritonitis. The question of intestinal wall or bladder wall involvement (by plastic adhesion or cancerous penetration) may be elucidated by gastrointestinal x-ray or cystoscopic examination as mentioned later. The distinction between Stage V (removable mass) and Stage VI (irremovable mass) can be definitely made only during operation. Though the preoperative findings of a large mass with extensive fixation may give the impression of irremovability, the point can be decided with certainty only after the abdomen is open.

Curettage.—The laboratory examination of the curettings establishes the diagnosis of corpus carcinoma, and the deeper pelvic palpation under the analgesia gives additionally accurate palpation findings to assist in determining the stage of development of the growth. The curettage furnishes information also as to the size and shape of the uterine cavity, and may give clear indications of a projecting large or small mass. The approximate location of a limited growth may sometimes be ascertained by noting at which part of the wall the thick curettings are obtained. An idea of the surface width and length of the growth may be revealed in the same way. A hint of the depth of the growth may be given by the thickness of the curettings and

before operation as far as possible with the various helps available. The six stages, each representing a definite extent of involvement, are as follows:

Stage I: Endometrium alone involved.

Stage II: Definite involvement of the muscular wall, but not beyond its middle.

Stage III: Extension to the outer half of the uterine wall, but not beyond the borders of the uterus. This includes extension to the peritoneal coat with possible areas of adhesive peritonitis, but without carcinomatous involvement of the adhesions.

Stage IV: Extension to surrounding structures but not beyond removable ones, such as adnexa and adjacent portions of the broad ligaments. There may or may not be extensive intestinal or other peritoneal adhesions, but no extension of carcinoma cells into such adhesions.

Stage V: Extension into structures not advisable to remove, but removal of the original tumor is still practicable. The carcinomatous extension may be into an adherent coil of intestine or an adherent area of bladder wall, or it may be along the broad ligament lymphatics into the deep structures of the pelvic wall.

Stage VI: There is such extensive involvement of surrounding structures that not even the main tumor mass can be safely removed.

Clinical Recognition of Stages.—Clinical recognition or identification of the stage in a particular case is useful in two ways, namely, in accurate reporting of the case and in selection of treatment for the patient. Identification of the stage of involvement for case reporting is a comparatively simple matter, because the report is made after treatment, and hence, in most cases the uterus is out and available for sectioning. Identification of the stage of involvement for the selection of treatment is a much more difficult matter, for it must be made before the uterus is removed. It is this last and difficult identification which I wish to discuss in particular.

There are a number of factors concerned in the early identification of the stage of involvement, early enough to be of assistance in deciding what treatment to give the patient. These factors are as follows: History of the case, pelvic examination, curettage-exploration of cavity and deep pelvic palpation under anesthesia, microscopic examination of curettings, and special examination methods, including gastrointestinal x-ray, cystoscopic examination, x-ray visualization of uterine cavity, and finally uteroscopy.

History.—This gives the time of onset of the symptoms, and the severity and progress of the same. This information indicates in a general way the age of the growth and the amount of tissue disturbance. However, possible errors of interpretation must be kept in mind. The first symptoms may have been due to some other condition, the endometrial carcinoma coming later. Likewise the severity of the symptoms may be due to some complication. Even though the bleed-

the masses projecting into it. However, such injecting of the cavity carries the danger of spreading the carcinoma to the peritoneal cavity through the tubes, and hence should not be used. Most of this information can be obtained during the curettage by careful use of curette-palpation, without the danger of spreading the carcinoma through the tubes. Uteroscopy with special endoscopic tubes has been used in these cases, but the conditions in the uterus make the field of vision limited and unsatisfactory. Most of the information thus furnished may be obtained incidentally in the curettage, making unnecessary this additional instrumental disturbance in the uterus.

CONCLUSIONS

There is presented here a definite and complete clinical classification of cases of carcinoma of the corpus. The grouping is into six stages, each stage representing an extent of involvement within fairly definite anatomic limits. The limits are capable of recognition and easy designation by the combination of operative and laboratory examinations. Stages III, IV, V, and VI may ordinarily be recognized at operation and Stages I, II, III, and IV may be recognized in the laboratory. The laboratory examination may identify even Stage V by critical examination of the gross specimen and selection of blocks at its margin where the cancerous extension to irremovable tissue was cut across in the operation.

Each stage has also a clinical significance of its own, bearing on treatment or prognosis. In Stage I, the prognosis is practically 100 per cent curable. The growth is so superficial that it has occasionally been removed by the diagnostic curettage. Radium treatment will almost certainly eradicate it, though of course x-ray therapy should be added on the general principle that there may be scattered cancer cells in the pelvis. As radium would eliminate the remnants of carcinoma remaining after the diagnostic curettage in Stage I, operation for removal of the uterus would not be needed if we could identify this stage with certainty. However, this stage cannot be distinguished from Stage II until the uterus is removed and sectioned. Consequently the treatment employed must be suitable also for Stage II, i.e., for invasion of the muscular wall, which means operative removal of the uterus in addition to radiation.

In Stage II the prognosis is still excellent with thorough radical treatment, which embodies widespread radiation plus radical operation. If in the preoperative examination there is no palpable enlargement of the uterus and no superficial tenderness, we are justified in assuming that the growth is still within the second stage, and may encourage the family accordingly.

In Stage III there should be distinct enlargement and irregularity of the uterus appreciable on examination. If the process has extended to the peritoneum, superficial tenderness of the corpus is present, and

by an appreciable cavity being felt with the curette after the curettage, keeping in mind, of course, that firm infiltration extends some distance beneath the soft tissue removed. Considerable information as to the contour of the uterine cavity, before and after the curettage, may be secured by careful manipulation of the end of the curette.

Microscopic Examination.—The microscopic examination of the curettings, besides establishing the diagnosis of carcinoma, assists toward identification of the stage of involvement in two ways. In the first place, muscular tissue may be found in the sections, and thick pieces give an indication of the depth of penetration, remembering that beyond the soft tissue removed in the curettage there is an area of firm infiltration.

In the second place, the pathologic diagnosis shows the cell type and arrangement (pathologic Grades 1, 2, 3, or 4), and this may furnish some indication of the age of the growth and hence of its extent. There is a tendency to think of the cell type of growth as a fixed and continuing type in each case. But it may represent only a certain age in the development of the carcinoma, and if we knew the age-significance of the microscopic type encountered in the diagnostic curettings, we would know how long the carcinoma had been growing in that uterus.

Of course, no one is going to let a discovered carcinoma continue growing in a human uterus to determine the changes of cell type. But we have a hint in the direction of such progressive cell changes in those cases in which a curetting shows endometrial hyperplasia and a second curetting after a year or two shows endometrial carcinoma. Another hint is the finding of different cell types in the same tumor. In one of our cases of corpus carcinoma, a single microscopic field showed pathologic Grades 1 and 4. In another case, the uterus was double and one horn showed endometrial hyperplasia and the other horn showed endometrial carcinoma. Perhaps some information on this point of progressive changes through different cell types and arrangement could be obtained by animal experimentation with inoculated uterine carcinoma.

Special Examination Methods.—A gastrointestinal x-ray series may furnish valuable help in establishing or disproving intestinal invasion in a suspicious case. It is well to take a preliminary plain plate for a check, as it may show some gland calcification or other calcification which might be misleading later. Also, the plain plate may show dim indications of tumor outline or density. Cystoscopic examination is advisable in cases of suspected bladder or ureteral involvement, and may provide information as to whether the association is cancerous invasion or only pressure by the mass.

Outlining of the uterine cavity by x-ray visualization with opaque material will show the distortion and irregularities of the cavity and

In all the stages, the combination of radiation treatment and operation is advisable, provided the patient is a good operative risk. In a handicapped patient thorough radiation is to be employed, and the addition of operation is to be considered along with the extent of the handicap. In such a case the additional risk of operation must be carefully balanced against the chance of cure by radiation alone. In Stages I, II, III, and IV, where there is still a very good chance of complete removal of all carcinomatous tissue, the additional chance of cure given by operation justifies taking considerable handicap risk. If we could before operation identify the strictly first-stage cases, it might be advisable to depend on radium and x-ray treatment to cure them. But as previously explained this distinction cannot be made till the uterus is out and sectioned, hence the treatment must be such as will be safe for deep extension into the muscular wall. In Stage V the definite diagnosis of carcinomatous extension to irremovable structures cannot be made till the abdomen is open, consequently operation is strongly indicated on the possibility that complete removal may be carried out. In Stage VI the preoperative diagnosis cannot exclude the possibility of removal of the main tumor mass, with corresponding benefit to the patient. Consequently even in late cases the chance of relieving pressure pains or prolonging life warrants taking considerable handicap operative risk.

In some of these complicated cases the poor general condition is due largely to anemia from the uterine bleeding. When the bleeding is stopped by curettage and radium treatment, the general condition of such a patient may improve sufficiently to remove the contraindication to operation. So the decision against operation in a handicapped patient is not necessarily permanent, for conditions may improve sufficiently later to make operation advisable.

In those cases in which the contraindication to operation is some serious continuing disease, the outlook for the patient is still far above the hopelessness of former times. In an encouraging percentage of these patients submitted to thorough radiation with radium and x-ray, the carcinoma has been cured, and this percentage is increasing with the increasing effectiveness of deep radiation and the increasing accuracy of its application to corpus cancer.

Six stages may at first thought seem a rather large number. It seemed so to me, and I studied a good deal trying to reduce the number. But carefully considered from the standpoint of accurate definition of each stage and the classification's usefulness in clinical and laboratory work, the six stages were found necessary. A reduction in number by combining any two of them was unsatisfactory. For example, if Stage I included I and II and the operator received a laboratory report stating "Corpus carcinoma, clinical Stage I," he would at once wish to know whether or not it had extended to the muscular wall, because of the difference in clinical significance. If

sometimes there is spontaneous pain from the area of local peritonitis. There may be some fixation of structures by peritoneal exudate involving intestinal or bladder wall. The prognosis is still good, provided radical treatment is employed promptly before the carcinoma cells penetrate the adhesions into intestinal or bladder wall.

In Stage IV there is carcinomatous extension beyond the uterus, but only in the broad ligament areas with possible involvement of ovaries or tubes. As these structures are removed in the regular radical operation the prognosis is still fair, though extensive broad ligament involvement naturally suggests the possibility of fine nonpalpable lymphatic extensions beyond. Intestinal adhesions are not of serious significance unless cancer cells have penetrated into them, and if they have so penetrated that puts the case in the next stage.

In Stage V the carcinomatous extension may be into an adherent intestinal coil or an adherent area of bladder wall, or it may be along the lymphatics into the deep structures of the pelvic wall. Resection of an intestinal coil or an involved area of bladder wall is, of course, possible, but under the circumstances it is not ordinarily advisable. Such palpable extension means usually deeper nonpalpable extension, for the eradication of which dependence must be placed on deep x-ray therapy, and it is well to depend on the radiation to take care also of the palpable visceral wall involvement. The additional chance of cure, if any, by resection is not sufficient to warrant the additional serious operative work, with its mortality and morbidity risks.

The plan of treatment in Stage V is to remove the main mass of tumor tissue by removing the uterus and adnexa. By this removal of the tumor, pressure symptoms are relieved and also the patient is given a better chance of cure or protracted relief by the x-ray therapy, because only scattered remnants of carcinomatous tissue remain to be dealt with. In this stage in which cancerous extensions must be left, supravaginal hysterectomy is usually preferable to complete, for the cervix is rarely involved, though occasionally circumstances may make the additional work for removal of the cervix advisable.

In Stage VI the definite distinction from the preceding stage is made at operation after the abdomen is open. Careful palpation all around the tumor and tentative attempts at separation of adhesions here and there, finally make it clear that the adhesions are carcinomatous instead of simply inflammatory and that the involvement is so extensive that safe removal is impossible. In such cases an attempt at enucleation is very likely to start uncontrollable hemorrhage. One or more specimens are excised from characteristic areas, with care to avoid bleeding which cannot be easily controlled by suture. In this stage the prognosis is of course bad in regard to cure, but deep x-ray therapy may control the growth sufficiently to keep the patient in fair comfort over a long period.

A REPORT ON RADIATION TREATMENT OF CANCER OF THE CORPUS AND CERVIX UTERI FROM THE BROOKLYN HOSPITAL*

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WE HAVE been using radium in the Brooklyn Hospital for the treatment of uterine cancer since Jan. 1, 1921. In the series covered by this report, all were treated prior to Dec. 31, 1929, so that more than five years have elapsed since treatment was instituted. In the nine years, we have treated 36 patients with cancer of the corpus, and 100 patients with cancer of the cervix uteri. Ward and private patients have been included in this report, and there have been several different operators.

In all of these cases the radium salt was used, contained in two 50 mg. capsules. The screens were a glass capsule containing the radium, a second capsule of platinum 1 mm. in thickness, and a rubber tube 2 mm. in thickness. One millimeter of platinum absorbs all the primary beta rays, and the emergent secondary beta rays are absorbed by the 2 mm. rubber screen, so that our patients have received only gamma rays. We are indebted to the late Dr. Harold Bailey of New York for the suggestion that we use 1 mm. of platinum as a screen, and that by so doing we would probably avoid some serious injuries.

Our general plan of treatment for carcinoma of the corpus was to do a diagnostic curetting and insert the radium capsules in tandem high up in the uterine cavity. The cervical canal and vagina were then packed with dry gauze. The initial radium dose was 2,400 mg. hours.

If the microscopic diagnosis on the curettings was reported as malignant, if the disease was clinically rather early, and if the patient was a proper operative risk, she was subjected to a total abdominal hysterectomy six weeks after radiation. The uterus was then studied microscopically to substantiate the diagnosis. If the disease was far advanced or if the patient was not a proper operative risk, she was not subjected to a hysterectomy, but was treated with a second or a third dose of radium within the uterine cavity.

In reviewing this material, great care has been exercised to include only cases in which a definite carcinomatous process was proved by careful histologic examination. In the instances in which the diagnosis was made from examinations of curettings, they were uniformly of sufficient bulk to insure that a genuine neoplastic process existed.

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Stage II were extended to include all muscular involvement, neither the clinician nor the pathologist would be satisfied with that broad designation, for each would wish to have stated clearly whether the cancer involved only a small part of the muscular wall or extended into the outer half. The same objection applies to any combination of two stages, and still more to any combination of three. Careful critical study of the six stages in practical application to clinical and pathologic work shows that each stage represents a definite step in the progress of the cancerous infiltration and is of importance to the clinician in treatment and prognosis.

Accurate records are necessary to reliable statistics. Accurate recording starts with the patient's history and extends through all phases of the conduct of the case. It is only thus that case records can be made valuable in assisting the physician in the selection of the best treatment for his succeeding cases and in furnishing published statistics from which reliable conclusions may be drawn. In the cases now under consideration, an important feature is the accurate recording of facts indicating the stage or extent of the growth. For this purpose attention must be given to careful examination and recording of findings before operation and then of gross findings during operation (including any disturbance or surrounding structures that may or may not be dependent on the uterine growth) and then of gross findings after operation in the examination of the specimen in the operating room and then of gross findings in the laboratory, where the specimen is divided in a systematic way and prepared for microscopic investigation.

Valuable information is often missed by failure to examine carefully or record accurately at one or more of the above mentioned phases of the case. There is an inclination on the part of the surgeon to depend on the laboratory report for all recorded information about a removed tumor, whereas its location and relations and attachment as determined during operation are important items, as are also its size, shape, color, and consistency before these are changed by the manipulations of operative removal or by incisions for inspection after removal.

We are engaged in the serious and difficult business of saving life, and for the solution of the intricate problems encountered, we need all the help we can secure by careful observation and accurate recording of findings in the various phases of these cases. And yet the opportunities for such observation and recording are often permitted to slip away, sometimes even without recognition. A city detective bureau which handled its opportunities as carelessly would not get very far in the detection of crime. We must seize every opportunity for observing and recording clues which may assist in the solution of our serious problems.

malignum (Grade II). A third patient was treated in 1924 with a 2,400 mg. hour dose of radium. Eight years later, in 1932, she showed signs of recurrence, and she was given a second 2,400 mg. hour dose. She is still living and well. She likewise had an adenoma malignum (Grade II).

The pathology in this group of 12 five-year cures is as follows:

5 Superficial adenoma malignum	Grade I
5 Adenoma malignum	Grade II
1 Adenocarcinoma	Grade III
1 Diffuse carcinoma	Grade IV

A comparative tabulation of carcinoma of the corpus cases with five-year cures is as follows: Memorial Hospital,⁸ 85 per cent; Henry Ford Hospital,⁹ 61 per cent; Washington University Hospital, St. Louis,⁴ 52 per cent; the Brooklyn Hospital, 33.3 per cent; and Department of Health, Cancer Division, Detroit,¹⁰ 28.6 per cent.

From Jan. 1, 1921, to Dec. 31, 1929, we treated 100 patients with cancer of the cervix. We have followed 79 patients, and 21 are untraced, so that our follow-up is 79 per cent.

In this group we have 12 patients who lived five years or more after treatment, so that our five-year salvage is 12 per cent. We have 8 patients who died between three and five years after treatment, 33 who died between one and three years, 26 who died under one year after treatment, and 21 are untraced, so that our mortality is 88 per cent.

In the group of 12 five-year cures, the cancer was of the epidermoid variety, except in one case which was a basal cell carcinoma. There was one Grade II, 9 were Grade III, and 2 were Grade IV. Only two of the patients received x-ray treatment.

Five of this group were subjected to a Byrne cautery operation, leaving only one and one-half to two inches of the corpus uteri in place. One 50 mg. radium capsule was then placed in the remains of the uterine canal, and a second 50 mg. capsule was placed crosswise in the crater. The initial dose of radium was 2,400 mg. hour.

Two of these five patients received a second radium treatment, and one of them had x-ray treatment in addition.

In order to do a Byrne cautery operation, the uterus must be movable. If the cervix is fixed by extension of the disease, it cannot be pulled downward and the procedure is impossible.

Three of these patients treated by the Byrne operation and radium had secondary hemorrhages about ten days after. Two are alive and well, one died six years after the operation from an anginal attack. Her pelvis was in excellent condition at the time of her death.

One of these patients has a vesicovaginal fistula a few months after her second radium treatment. No attempt has been made to repair it.

One patient had a cautery amputation of the cervix immediately prior to her treatment with radium. Only one inch of the cervix was removed, so that the amputation cannot be classed as a Byrne operation.

Six of the group received radium alone, and in one, x-ray was given in addition to radium.

Two of them had only one radium treatment, and four received more than one treatment.

In this group of six patients, there was too much fixation of the uterus to attempt to do a Byrne operation.

Of the three patients treated by radium and a Byrne operation, one lived two years, one lived one and one-half years, and the third was untraced. Of the two patients treated by radium followed by total hysterectomy, one was given 3,600 mg. hr. of radium in 1923, and three months later a total abdominal hysterectomy was

In the great majority of cases in corpus carcinoma, the uteri were subsequently examined and the findings in the curetted material were confirmed. No doubtful cases and none of adenoma destruens have been included, even though they have had radium treatment and a total hysterectomy, because we do not consider this to be a real cancer case.

Grade I	Superficial papillary adenoma malignum
Grade II	Adenoma malignum
Grade III	Adenocarcinoma
Grade IV	Diffuse (anaplastic) carcinoma

In this analysis of corpus carcinoma cases we have used the following classification of Mahle, later confirmed by Healy.¹ This classification has lately been used by Newell and Crossen⁴ in their report on corpus carcinoma.

In explanation of the above classification as employed in this report it may be stated that tumors, classed as superficial papillary adenoma malignum, have uniformly been diffuse forms of the disease, and no examples of the circumscribed lesion have been encountered.

RESULTS

The corpus carcinoma group consists of 36 cases. Complete follow-up data are available in 31 cases, and 5 patients are untraceable. The follow-up percentage is therefore 84 per cent.

Twelve of the patients lived five years or over, and 24 did not live five years, or were untraced. The five years salvage, therefore, is 33.3 per cent, and the mortality is 66.7 per cent.

A study of the 24 patients who died under five years shows that 5 patients are not traceable. Of the remaining 19 patients, one died two days after hysterectomy from acute cardiac dilatation, and another patient died seven days after operation from general peritonitis. This was one of the first cases in the series, and the hysterectomy was done ten days after radiation. A third patient died in nine days from embolus.

The primary mortality, therefore, is 8.33 per cent. Of the remaining 16 patients, 6 were hopeless. They had one radium treatment with or without x-ray treatment, and died within ten months. The remaining 10 patients were advanced cases and lived from one to three and one-half years. Five of these had radium alone, 4 had radium and hysterectomy, and 1 had radium and an exploratory laparotomy. The pathologic diagnosis on these 19 deaths were advanced adenocarcinoma, with the exception of one case which was a myosarcoma.

A study of the 12 patients, who lived for five years or more, reveals that two died six years after radiation alone, and 1 is living eleven years after radiation alone. Three patients are living twelve years after radiation and total hysterectomy, 1 nine years after, 4 are living eight years after, and 1 patient is living and well, fourteen years after radiation and hysterectomy.

In this group, 9 had radium and hysterectomy, and 3 had radium alone. Of the 3 patients who had radium alone, it is interesting to note that one patient had three doses of radium totaling 7,200 mg. hours, and died of carcinoma six years after the first treatment. Her pathology was adenoma malignum (Grade II).

Another patient had four doses of radium totaling 7,200 mg. hours, and died of carcinoma six years after the first treatment. The pathologic diagnosis was adenoma

The cases covered by this report have received only gamma rays from two 50 mg. capsules of radium. The initial dose was 2,400 mg. hr., followed by one or more doses. Only a very few cases have had bladder or rectal injury.

Our present plan for treatment of carcinoma of the cervix is:

a. A diagnostic biopsy, so that we may know the type of disease and its radio-sensitivity.

b. An x-ray cycle consisting of 4,800 to 7,200 r. units, screened by $\frac{1}{2}$ to 2 mm. of copper with a distance of 50 to 80 cm. through 4 to 6 ports. The daily dose is 200 to 300 r. units through two ports. The total number of daily treatments covers a period of two or three weeks.

c. Ten days later the patient is treated with 3,600 to 4,800 mg. hr. of radium at one treatment within and around the cervix. The screening is 1 mm. of platinum and 2 mm. of rubber.

Carcinoma of the corpus is treated by a diagnostic curettage, and a 2,400 mg. hr. dose of radium within the uterine cavity. An x-ray cycle follows, and if the patient is operable, a complete hysterectomy is done six weeks later. If the patient is inoperable, radium and x-ray treatments may be repeated in six weeks or two months.

The question of radium and x-ray dosage is in a state of flux. The treatment of yesterday is obsolete, and that of today will probably be changed in the future.

Research institutions for the treatment of cancer are justified in using large doses of radium and x-ray, because they must lead the way in the treatment of this disease. I feel very strongly, however, that the general hospital is not justified in using such large dosage until the treatment has become standardized. The late effects of these large doses of radium and x-ray are too serious. I am convinced that it is better to cure a smaller number of cancers than to have a larger percentage of cures and many patients who are invalids from fistulas and damage to the abdominal organs.

A majority of the advanced cancer patients will die soon enough from the disease, without these serious added complications.

The Byrne cautery operation has been an excellent adjunct to our radium treatment of cancer of the cervix. It is only applicable, however, to the very early case, that is, to the case when there is no fixation of the uterus. So few of the cases are early ones, that the Byrne operation has a very limited field.

In this small series of cases, the disease has been far advanced before the patients presented themselves for treatment. I make a plea for more and more education of the public and physicians, so that the patients may learn to consult their physicians at the first symptoms of the disease, and the physician may learn to recognize the condition as early as possible, or if in doubt, send the patient to an institution where a competent diagnosis may be made.

done. There was a recurrence in the scar of the vault of the vagina three years later, together with metastasis in the ilium. She was then given x-ray treatment but she died one year later.

The second patient received 2,400 mg. hr. of radium in 1925. A total abdominal hysterectomy was done two months later. This patient lived two years.

Of the three other patients in this group who had x-ray, one was treated by cauter, radium, and x-ray treatment. She lived four years.

This patient developed a vesicovaginal fistula which was repaired at the Woman's Hospital in New York two years after her initial treatment. The fistula remained healed for about one year, then it opened as the disease began to progress rapidly.

A second patient had cauter, radium, and x-ray treatments and lived two years. The third patient was treated with radium and x-ray. She lived nine months.

The patient who developed a rectovaginal fistula had an advanced epidermoid carcinoma. Her cervix was coned out with cauter, and she was given 3,850 mg. hr. of radium in two doses. She lived two years.

The incidence of cancer in the stump of the cervix in our series was as follows:

1. Supravaginal hysterectomy for fibroid twenty-one years before. Given radium and lived one year.
2. Supravaginal hysterectomy for fibroid twenty years before, given radium, untraced.
3. Supravaginal hysterectomy for fibroid fifteen years before. Lived one year after radium.
4. Supravaginal hysterectomy for fibroid fourteen years before. Lived one year after radium.

Incidence in our series, 4 per cent; mortality 100 per cent.

It is interesting to note that Healy¹ finds that the incidence of carcinoma of the cervical stump at the Memorial Hospital in New York is 2.6 per cent, and that his five-year salvage is 14 per cent.

Von Graef² has published a comprehensive report on this subject from a collected series of 4,269 patients with cervix cancer. He found an average incidence of stump cancer to be 4.1 per cent. He makes a plea for total hysterectomy, instead of supravaginal hysterectomy, as a prophylactic measure.

Pearse³ contends that the possibility of carcinoma developing in the cervical stump should not be considered as an indication for total removal of the uterus, unless the mortality for the total hysterectomy can be shown to be the same as it is in the supravaginal operation.

Healy¹ states: "The low incidence of stump carcinoma does not justify risking the increased mortality of total hysterectomy instead of the subtotal operation to prevent the later occurrence of cervix cancer in all patients from whom the uterine corpus is to be removed."

A comparison of five-year cures in the patients with carcinoma of the cervix, in our series with the results in other hospitals is as follows: Henry Ford Hospital,⁴ 52 per cent; Woman's Hospital,⁵ 25.8 per cent; University of Pennsylvania Hospital,⁶ 25.1 per cent; Washington University Hospital,⁷ 23.9 per cent; Memorial Hospital,⁸ 22 per cent; Jefferson Hospital,⁹ 18.4 per cent; Department of Health, Cancer Division, Detroit,¹⁰ 13.2 per cent; and the Brooklyn Hospital, 12 per cent.

The five-year cures in this series of cases of cancer of the corpus and cervix uteri are considerably lower than the five-year cures reported by several other institutions.

Several of our patients had clinical symptoms of cancer. They were treated for it and are alive and well, but they are not included in this report because the diagnosis was not substantiated by the microscope.

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DISCUSSION

DR. WILLIAM A. JEWETT.—When the reports from five clinics in different parts of the United States give five-year cures of carcinoma of the body of the uterus varying from 85 per cent to 28.6 per cent, and reports from eight clinics show a difference of from 32 per cent to 12 per cent in five-year cures in carcinoma of the cervix, all of them presumably following about the same line of treatment, it is evident that there is need for greater uniformity in the method of compiling statistics, in the standards of tumor grading and for a widespread improvement in our methods of follow-up. Dr. Smith is to be congratulated on his success in having kept track of over 80 per cent of his cases. In a recent review of my own personal cases I was less fortunate and was able to obtain but a little over 50 per cent of the end-results. This poor showing was due in part, I believe, to the fact that my patients were not all cared for in the same institution, and to the further fact that many of my cases, being referred cases, were returned to their own physicians, and from whom, for one reason or another, it was impossible to obtain a satisfactory account of the subsequent history. If the calculation of the percentage of five-year cures is based on the number of definitely followed-up cases, it will give a much higher figure than will be found if the untraced patients are assumed to be dead, as Dr. Smith has done in his report. Unless the same method of procedure is followed out universally, it is impossible to evaluate one's own results of treatment by comparison with the figures of others.

When different methods of grading of the tumors are practiced, Smith's suggestion that gynecologists throughout the country adopt a uniform scale is a good one.

The problem of providing a satisfactory workable follow-up system is difficult and likely to involve the expenditure of a considerable amount of money if it is to succeed. Still it is important for we must know the results of our particular type of treatment as well as the results obtained by others if we are to give our patients the best possible care and if we hope to salvage a larger number of those who are afflicted.

Smith has spoken of the great benefit to cancer patients if each hospital treating this disease should establish a tumor clinic along the lines suggested by the American College of Surgeons. I am heartily in accord with this suggestion provided the hospital is equipped with the necessary amount of radium and has an adequate x-ray therapy machine. Such a tumor clinic has been organized at the Caledonian Hospital and has been functioning for several months. The sessions are held once a week, and there is present a representative of each of the major departments of the hospital—the pathologist, the roentgenologist and a stenographer. The patient is presented by his own physician, is examined by a number of those present, and after he has retired there is a general discussion of the problem presented and a course of treatment is outlined. So far there have not been many cases of pelvic cancer, and naturally it will be a long time in such a young clinic before any statistics are available; but I mention the working of this clinic to show that not "fewer doctors" but more doctors are being trained in the observation and treatment of cancer.

It would be of great benefit to cancer patients if each hospital treating this disease would organize a tumor clinic along the lines suggested by the American College of Surgeons. The patient would then be under the observation of the same group of men in the outpatient department, the ward, the operating room, and in the follow-up clinic.

The drawback to the plan, however, is that it takes these patients out of the general ward service, and far fewer doctors are trained in the observation and treatment of cancer.

I contend that all doctors must be trained to recognize cancer in the early stages. To this end, I suggest that each gynecologic service should have one clinician trained in the treatment of cancer who would be constantly in charge of the service cancer cases.

The pathologist and radiologist would work with him.

The other members of the gynecologic staff would serve as active workers in the group for a definite period of rotation. In this way, the patients would benefit from being constantly under the observation of a cancer expert, and all the staff would benefit from a period of observation of cancer and a study of its treatment.

The clinician in charge of such a group must, of course, be interested in the treatment of cancer. His continuous observation and care of the cancer patient would be far more valuable than the "hit or miss" plan of allowing the patient to be treated by the staff member who happened to be on service. Likewise his teaching of internes and staff members would be invaluable.

I am of the opinion also, that the doctor in charge of a private patient would be only too glad to consult this group of specialists in regard to the treatment of his patient, and that he would follow their suggested plan of treatment.

The statistical study of cancer would be much more valuable if all observers followed the same standards of tumor grading.

I have recently learned that members of the American Urological Society may send slides to the Surgeon General's office at Washington for grading. This is a step in the right direction, and in the near future I hope that gynecologists may all follow a similar standard of tumor grading.

Radiosensitivity is still something that depends too much on the personal equation of the pathologist to be of great value. It is possible that in the future much more may be known about it; then perhaps, the radiosensitive tumor may be treated by radium and x-ray, and the radiononsensitive tumor may be treated by surgery. I think, however, that only those men who are able to do master surgery can ever hope to cure cancer by this means.

I am greatly indebted to Dr. James W. Decker, who has graded all the sections, and to Mrs. Hallen, who has done so much of the follow-up work.

ORAL PARALDEHYDE ADMINISTRATION IN OBSTETRICS

SUPPLEMENTING PENTOBARBITAL AND PANTOPON AS AN ANALGESIC AND AMNESIC IN LABOR

A PRELIMINARY REPORT OF 50 CASES

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RECENTLY there have been many reports in the literature advocating the use of paraldehyde for the relief of pain during labor, the method of administration being per rectum.^{1, 3-7} We have used paraldehyde rectally in this clinic for nearly two years, the technic differing from that of Colvin and Bartholomew³ only in that sodium pentobarbital was substituted for sodium amytal because it seemed to cause less excitement. A careful study of these cases would tend to show that paraldehyde in combination with one of the barbiturates is superior to any other method of obstetric anesthesia and analgesia. The possibility of oral administration was investigated in order to avoid the disadvantages of the rectal route among which were: (1) the difficulty of placing the drug above the presenting part; (2) the tendency of the patient to expel the preparation; (3) the comparatively slow absorption time; and (4) the inadvisability of doing rectal examinations following medication. A review of the literature revealed no experimental work along this line.

The principal task to overcome before paraldehyde could be administered orally was to mask the disagreeable odor and to make the preparation as palatable as possible. The Department of Pharmacology was consulted and they suggested mixing the active ingredient with propylene glycol, alcohol, and syrup of acacia.

Propylene glycol has commanded comparatively little or no interest in medicine. Experimentally⁹ it has been studied in animals and proved to be absorbed, and to give rise to additional glycogen storage in the liver. Toxic effects were noted only when enormous quantities (the equivalent of 2 pounds daily for a 70 kgm. man.) were given. The toxicity apparently comes from pyruvic and lactic acids, inter-

mediary products of oxidation. Propylene glycol, $\text{CH}_2-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\text{CH}_2-\text{OH}$, in its pure

form is colorless, odorless, and has an acid and sweetish taste. It is miscible with water, glycerol, methyl and ethyl alcohols, acetone, ether, chloroform and ethyl acetate. Paraldehyde is very soluble in propylene glycol and at the same time

My method of applying radium has been similar to the one described except that instead of screening the radium with 1 mm. of platinum and 2 mm. of rubber I have used $\frac{1}{2}$ mm. of silver, 1 mm. of brass, and 1 or 2 mm. of rubber. Dr. Smith has made use of the Byrne cantery operation in a considerable number of his patients; a procedure that I have not used at all, and he has made less use of the x-ray therapy than has been our custom. However, I note that his present plan of treatment of carcinoma of the cervix includes an x-ray cycle prior to the application of radium. Our system of grading tumors is the same as that used at the Brooklyn Hospital, and I find about the same proportion of cases falling in each group. In one of our fundal cases we found both a papillary adenoma malignum and a sarcoma.

DR. CAMERON DUNCAN.—At the Kings County Hospital, we take care of these cases in the Gynecological Service, a system which has, I think, certain advantages.

X-ray and radium are combined now in most clinics, but I believe that there is a certain field where surgery should be added. Taussig has shown this in a number of lymphadenectomies. The reduction of the blood supply, and the lymphatic block might be of advantage in a good many cases.

The clinical stage in relation to the pathologic grades is highly important. For example, a clinical Stage I of carcinoma of the cervix, with only a small portion of the cervix involved, has a much better chance than a Stage II or Stage III case where it is beginning to spread to the parametrium, regardless of the pathologic grading. A case that is absolutely radioresistant, that is, if the lesion does not melt away from the cervix within two months' time after the initial radiation, and if the disease has not spread too far, is, I believe, one in which radical surgery is indicated.

DR. SAMUEL L. SIEGLER.—In the Gynecological Clinic of Dr. Jacob Halperin at the Brooklyn Woman's Hospital, we insist on a routine endometrial biopsy of all cases of menstrual dyscrasia. In the last two months, two young women who presented themselves, complaining of sterility and menstrual disturbances, were found as a result of endometrial biopsy to have an adenocarcinoma of the fundus of the uterus. Both patients were in the early thirties, one twenty-nine, and the other thirty-two years of age.

I would strongly urge the adoption in gynecologic clinics of frequent endometrial biopsies on all patients who present some menstrual disturbance. The procedure is a simple one and the result will amply justify the little pain that it may cause the patient.

DR. WILLIAM SIDNEY SMITH.—In answer to Dr. Duncan, I may say that we did not make any clinical groupings of these cases, but I believe that it might be very valuable.

I wonder if the secret of the treatment of cancer in the future may be that some one will discover more about radiosensitivity. If they do, it is quite possible that the radioinsensitive tumor may be turned over to the surgeon, and the radio-sensitive tumor may be treated by radium and x ray. That plan may have possibilities for the future, but at present we do not know enough about it.

Not so long ago I was listening to some reports of cancer from a well-known institution. The frequency rates were rather high. Later, a slide was put on the screen showing the damage that had been done to these patients, and the number of ectocervical fistulas, rectovaginal fistulas, and abdominal damage which had occurred. The damage was tremendous. In other words, while they may have had a large number of cancer cures, there were certainly a large number of maimed patients.

EXPERIMENT

The 50 cases studied represent practically consecutive admissions to the ward of patients that were early in the first stage of labor or were hospitalized before labor commenced. Of the 50 cases 37 were primigravidas and 13 were multigravidas. Eleven of the patients were private patients and 39 were free ward patients. Distribution between the colored and white race is shown in Table I.

TABLE I

	PRIMIGRAVIDAS	MULTIGRAVIDAS
White	26	11
Colored	11	2

The ages ranged from a fifteen-year-old colored primigravida to a thirty-eight-year-old white multigravida. The average age for the group was twenty-three years.

In this series of cases one observes considerable pathology, as in this clinic abnormal patients are received from many sources. The various complications have been outlined in Table II.

TABLE II

COMPLICATIONS	NO. CASES
Preeclampsia	8
Nephritic toxemia	2
Condyloma acuminata	1
Elephantiasis vulvae	1
Active syphilis	1
Cardiac	1
Breech presentation	2
Twin pregnancy with hydramnios	1
Acute yellow atrophy of liver	1
Postpartum hemorrhage	1
None	31
Total	50

The cervix at the time of paraldehyde administration averaged 6.25 cm. (minimum of 4 and maximum of 7) dilatation in the primigravidas, and 4.75 cm. in the multigravidas (minimum of 3 and maximum of 6). The station of the presenting part varied from low to midpelvis.

It is routine in this clinic upon all primigravidas to do an elective low forceps and episiotomy when the head reaches the perineum and the cervix is completely dilated. The type of delivery is shown in Table III.

While it is true that with the increase in the use of obstetric analgesia, there has been a corresponding increase in obstetric operations^a and a rise in maternal mortality and morbidity, we believe that these are both unnecessary, and that spontaneous delivery is just as pos-

its taste and odor are masked. The syrup of acacia with its pleasant vanilla taste holds the foregoing in suspension. The ethyl alcohol is added to increase the solubility of paraldehyde in the glycol.

Paraldehyde, the active agent for amnesia, enjoys a wide margin of safety between the toxic and therapeutic doses (a case has been reported³ where a genitourinary patient received 8 ounces from a misinterpreted order for 8 drams with recovery following nineteen hours of deep sleep). Knoepfel² states that it is a safe and promptly acting hypnotic hindered only by its unpleasant taste and odor on the breath. Six to 9 drams is the usual rectal dose in labor and after experimenting 5 drams was found to be the most satisfactory dosage for oral administration.

TECHNIC

Throughout the first stage of labor all of the patients were kept comfortable with sodium pentobarbital (gr. $1\frac{1}{2}$ to $7\frac{1}{2}$) and pantopon (gr. $\frac{1}{6}$ to $\frac{1}{3}$). We have always considered these to be excellent sedatives for the first stage of labor and have considered them, as have Rosenfield and Davidoff¹ in the original work, as necessary adjuncts in the preliminary preparation for paraldehyde. Patients can usually be quieted by this method, and it is only when delivery is becoming more imminent and pain approaching intolerability that paraldehyde is resorted to. We do not feel as the original workers later report⁴ that 6 to $11\frac{1}{2}$ gr. of the pentobarbital of sodium is advisable. We found that the average dosage of 3 or $4\frac{1}{2}$ gr. of sodium pentobarbital and $\frac{1}{6}$ gr. of pantopon was satisfactory.

Patients always met the following criteria before the paraldehyde could be given: (1) Regular contractions with a frequency of less than five minutes, (2) contractions lasting forty seconds or more, (3) cervix thinning out and dilating to 3 or 4 cm. in the multigravida and 5 to 6 cm. in the primigravida, (4) the head descending well into the pelvis, and (5) delivery apparently imminent in three or four hours.

A solution of 50 per cent paraldehyde, 40 per cent propylene glycol, and 10 per cent alcohol (90 per cent) was made up and stored in a refrigerator as was the syrup of acacia (N.F.). Ten dr. of the paraldehyde-glycol mixture (equivalent to 5 dr. of paraldehyde) were briskly stirred with 20 dr. of the syrup of acacia immediately before administration. The patient was told she was to receive a syrup that would produce sleep. The naris were loosely plugged with pledgets of cotton and the patient asked to swallow the half glassful of syrup quickly. This was followed by a few swallows of water and the patient allowed to recline. The cotton was then removed from the naris.

noted. Rectal variations are probably due to depleted circulation of the lower bowel by the encroaching head. It was not necessary to avoid noise and motion to produce sleep as was the case with rectal paraldehyde.

Complete amnesia, the desirable objective during labor, was present in 94 per cent of the cases. The primigravidas averaged two hours and thirty minutes without memory before delivery (a maximum of seven hours and minimum of thirty minutes). The multigravidas averaged one hour and fifteen minutes of amnesia prior to delivery (a maximum of four hours and a minimum of thirty minutes). Analgesia even with partial amnesia was obtained earlier by the preliminary medication of all cases.

Amnesia following delivery averaged seven hours for the series. This was of benefit to the new mother for the early uncomfortable hours of the puerperium were passed in sleep. Twelve patients were amnesic for ten hours; 1 patient, along with natural sleep, was amnesic for twenty hours; 3 patients recalled being taken from the delivery table one hour postpartum. Drowsiness with unconcern and disorientation persisted for twenty-four hours in nearly all cases.

Restlessness was present to only a small degree and sideboards were used on the bed but no other special care was given. Cooperation was frequently present with the patient responding to directions and often it was possible to administer postpartum drugs by mouth.

The average duration of labor for the primigravidas was thirteen hours and four minutes with a maximum of twenty-seven hours and a minimum of six hours. The multigravidas averaged nine hours and fifteen minutes, 2 of them having fifteen and seventeen hours of labor due to irregular and vague contractions early in the first stage. The shortest labor was three hours and thirty minutes.

We were unable to measure uterine contractions as did Moore and McCurdy⁷ by means of Dodek's hysterograph, but it is quite probable that there was a temporary decrease in the intensity and frequency for the first thirty minutes. This decrease, if present, is compensated for by regular, more intense, normal contractions later. The development of uterine inertia was grossly observed in only one patient. This undesirable relative effect was shown by complete cessation of contractions for a period of four hours and then labor was resumed with delivery three hours later. No pituitrin nor oxytocics of any sort were resorted to prior to delivery. The greatest aid in overcoming uterine inertia is the prevention of it by following the criteria suggested earlier in this paper. Keeping the patient on her back helps to maintain the expected type of labor.

Expulsive efforts of the mother were not abolished and appeared more pronounced in the cases having had the drug for more than three

TABLE III

METHOD OF DELIVERY	NO. CASES
Low forceps	25
Spontaneous	10
Midforceps including 2 manual rotations of head	4
Breech extraction	2
Total	51 (1 set of twins)

sible when the patient has been made comfortable with paraldehyde as when nothing is used. On the other hand, it has been proved very conclusively that episiotomy and outlet forceps in competent hands decrease rather than increase the risk to both mother and child. Supplemental anesthesia was used as shown in Table IV.

TABLE IV

ANESTHESIA	NO. CASES
Nitrous oxides	35
Local infiltration	4
Ether (cardine)	1
None	10
Total	50

Additional operations at the time accounted for the increase of supplemental anesthesia. All cervixes were inspected routinely and all multigravidas had an elective posterior repair of the outlet. Spontaneous deliveries and minor repairs of perineal lacerations require no supplemental anesthesia.

TABLE V*

OPERATIONS	NO. CASES
Elective trachelorrhaphy	15
Elective perineorrhaphy	11
Episiotomy	25
Repair of third degree laceration	1
Hysterotomy	1

*Oral paraldehyde was used for a low cervical resection as a local anesthetic in a patient with cephalopelvic disproportion and fulminating pre-eclampsia with good results, but this case is not included in the series.

RESULTS AND DISCUSSION

The disagreeable taste and odor of oral paraldehyde were satisfactorily disguised. Forty of the patients stated that this was an entirely new-tasting medicine and not unpleasant; the other 10 complained of bitterness, sweetness, or a slight burning sensation.

The absorption time was rapid by oral administration in contrast to the rectal method. Memory fled in five to ten minutes after the preparation was swallowed. No great variations in time of absorption were

The auscultation of the fetal heart during labor in all cases did not present any extraordinary change in rate or rhythm that disturbed the accoucheur. The estimated blood loss for the series in general was not increased. One patient, a twenty-two-year-old primipara, had a postpartum bleeding of 800 c.c. due to a persisting atonic uterus, but had an uneventful recovery.

The failures in this series (6 per cent) were due to vomiting of the preparation. Five patients were previously nauseated and vomited the paraldehyde. Three of the five had a second dose administered and two of them retained it with satisfactory results. Nausea accompanies the latter third of many labors and is an inconvenient feature to handle. After vomiting, many patients are able to retain a small amount, and it is because of this latter fact that we feel a second dose can successfully be given. Rectal paraldehyde can always be resorted to if nausea is extreme. The early administration of bicarbonate of soda aids the stomach in emptying, thereby preparing it for oral paraldehyde.

Blood Pressure

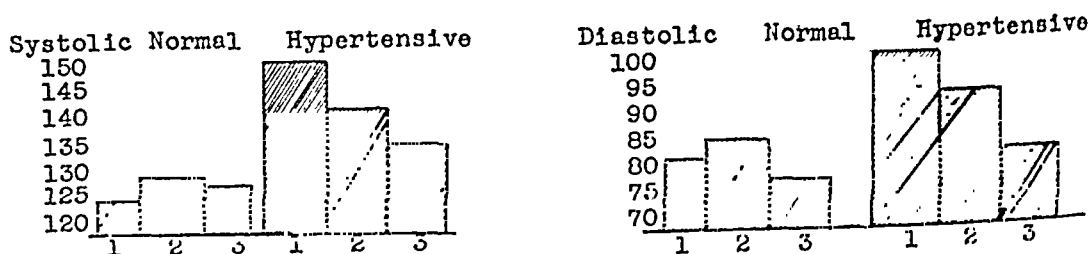


Chart 2.—Effect on blood pressure in 38 normal and 12 hypertensive cases: 1, onset of labor; 2, one hour after paraldehyde administration; 3, one hour postpartum.

One patient in the series had a delayed shock postpartum, from which she recovered but died on the fifth day. The autopsy diagnosis was acute yellow atrophy of the liver, a condition which was not felt to be due to either the paraldehyde or the propylene glycol, but was considered an accidental complication.

There was one stillborn, macerated infant, in a mother with a positive Wassermann. Intrauterine death was discovered before labor and therefore we can disregard it. Two babies required resuscitation. Mucus aspiration was all that was necessary in one; the other baby required artificial pulmonary insufflation for three minutes; both babies were crying healthily in ten minutes. The other 48 babies cried spontaneously on birth and all conducted a lusty neonatal period in the hospital until discharge. Not a single so-called "sleepy baby" was observed.

hours. Since 20 per cent of the cases delivered spontaneously, it clearly shows that this reflex remains present and the drug is efficacious in home deliveries of multiparas where operative intervention is not considered. No special nursing care is necessary, but the patient should be watched throughout her labor. The attendant need only be someone with sufficient ability to keep the patient from rolling out of bed. Restlessness is sometimes present, but we have not encountered any cases of active delirium.

We found no unusual nor unexpected change in the pulse, respiration or blood pressure. The pulse was elevated moderately as shown on Chart 1. The average pulse at onset of labor was 86, one hour before the paraldehyde and at the administration all were below 100 per minute except 2 cases. One hour after the taking of paraldehyde 12 were above 100 (the highest was 140 per minute in a case of prolonged labor). At delivery and one hour postpartum 12 and 18, respectively,

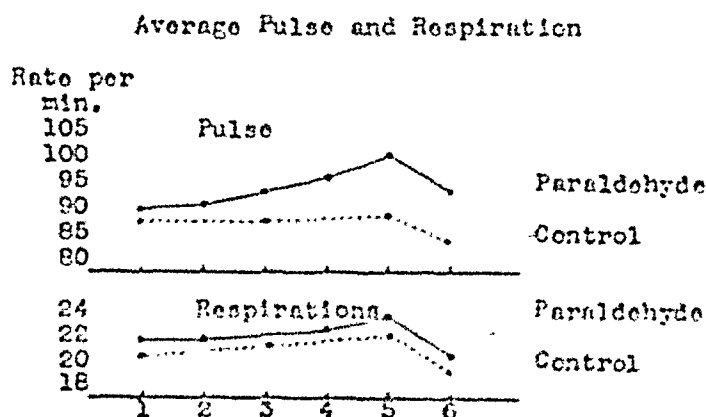


Chart 1.—Pulse and respiration 1, onset of labor; 2, one hour before oral paraldehyde; 3, time of administration; 4, one hour after administration; 5, delivery; 6, one hour postpartum. The control curves represent 50 normal, spontaneous deliveries.

had pulses above 100. The highest pulse was 144 in a case of twins and hydramnios one hour postpartum. All tachycardias seemed to parallel the type of operative or shocking delivery rather than arise from paraldehyde. The average respiratory rate was twenty-one per minute and no cases exhibited depression or poor ventilation as shown in Chart 1.

The blood pressure had a general tendency to fall in patients with systolic above 140 mm. of mercury and a tendency toward elevation for those below 120 mm. of Hg following paraldehyde administration. Two cases of preeclampsia, whose blood pressures were 170/120 and 170/110 at the onset of labor, fell to 141/94 and 160/90, respectively, one hour after the paraldehyde was given. One hour postpartum these pressures were 132/74 and 140/84, respectively. There were but 3 readings below 100. The effect of paraldehyde on patients with normal blood pressure and with hypertension is shown in Chart 2.

Peckham, 79 per cent in 2,550 cases; while Tracy's patients showed an incidence of 90 per cent cervical laceration. In this series there was an incidence of 48.7 per cent of cervical laceration demonstrable six weeks postpartum.

For the purpose of classification we have divided the cervical results into five groups:

Grade A, No demonstrable cervical injury.

Grade B, Superficial laceration healed spontaneously 6 weeks postpartum, or erosion, or both.

Grade C, Unilateral lacerations sufficient to produce definite cervical deformity, estimated depth $\frac{1}{2}$ cm. or greater.

Grade D, Bilateral lacerations of estimated depth of $\frac{1}{2}$ cm. or greater.

Grade E, Stellate lacerations of $\frac{1}{2}$ cm. or greater.

TABLE I. INCIDENCE OF CERVICAL INJURY

CHARACTER	GRADE	NO. CASES	PERCENTAGE		
Normal	A	72	37		
Erosion	B-35				
Superficial	B-48	75	39	Satisfactory	76%
Unilateral	C	24	12		
Bilateral	D	19	10		
Stellate	E	3	2	Unsatisfactory	24%
Totals		193	100		

As a further criterion of the severity of this classification, let it be said that only six of the lacerations were of sufficient depth to cause a definite eversion of the cervical lips.

In no case was pituitrin used until the completion of the third stage of labor. In no case was a manual or instrumental dilatation of the cervix done.

For purposes of simplification in our further studies those cervixes Graded A and B were considered satisfactory, since Grade B is the type of injury which readily responds to office cautery. Grades C, D, and E are listed as unsatisfactory cervical results.

MALPOSITION

It is our custom to divide retrodisplacements into three different classes:

First Degree Retroversion.—A backward rotation of the uterus on an imaginary axis passing transversely through the cervico-fundal junction so that the fundus points toward the promontory of the sacrum.

Second Degree Retroversion.—A backward rotation in which the fundus points toward the hollow of the sacrum.

Third Degree Retroversion.—In which the fundus points toward the culdesac. In second and third degree retroversion there is commonly associated a retroflexion, or bending backward of the fundus on the axis of the cervix. In this study all patients with second or third degree retroversion showed a concomitant retroflexion and in this classification no separate distinction will be made.

CONCLUSIONS

A paraldehyde-propylene glycol mixture has been administered orally in a series of 50 cases and has proved to be a successful, simple, non-expensive agent for the relief of pain in labor. A prolonged amnesia resulted which carried no deleterious effects to either mother or infant.

It is realized that with this small series of cases, one cannot give decisive conclusions. A more complete study is now under way.

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THE PRIMIPAROUS INTERNAL GENITALIA AFTER FORCEPS DELIVERY*

A FOLLOW-UP STUDY OF CERVICAL LACERATIONS AND MALPOSITION

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(From the Philadelphia Lying-In Hospital)

THE present paper deals with the lesions of the internal genitalia found at follow-up examination six weeks postpartum in 193 ward primiparas delivered by forceps at term and is intended as a companion study to a previous report made to this Society on "The Primiparous Perineum After Forceps Delivery." The statistics are taken from the same group of patients. The purpose is a further attempt to answer the question, "What Price Maternity?" from the standpoint of non-febrile morbidity. In this report the term "internal genitalia" includes the uterus and adnexa.

The number of cases studied is comparatively small. But it is believed that a careful analysis of the available material indicates definite trends. And as such an index serves a useful purpose.

Modern medical literature shows a surprising lack of statistical uniformity in the incidence of cervical lacerations.

Reporting primiparas only, Galloway found an incidence of 15.8 per cent in 500 cases; Aldridge and Watson 34 to 46 per cent in 2,800 patients; Barrett, about 50 per cent unsatisfactory cervical results; King, 78 per cent in 183 patients;

*Read at a meeting of the Obstetrical Society of Philadelphia, October 1, 1936.

The patients delivered by low forceps showed the highest percentage of satisfactory results for two reasons: They had easier parturitions and less cervical trauma in delivery.

The postural results bear out the opinion of Plass and Lynch that forceps delivery is apparently unrelated to the incidence of malposition.

RELATION OF AGE TO CERVICAL INJURY AND MALPOSITION

In the patients studied the best results were obtained in the twenty-five to twenty-nine-year old group. The good result is attributable to the fact that these

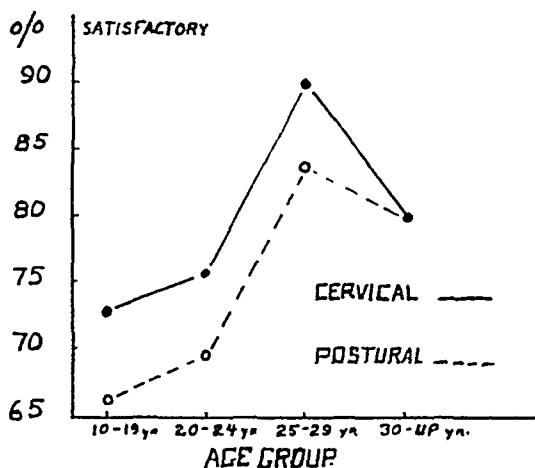


Fig. 1.

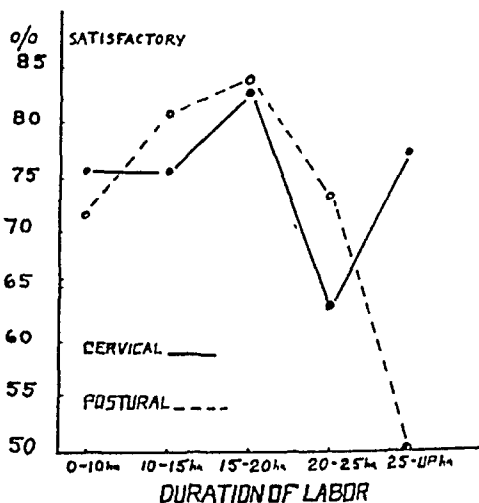


Fig. 2.

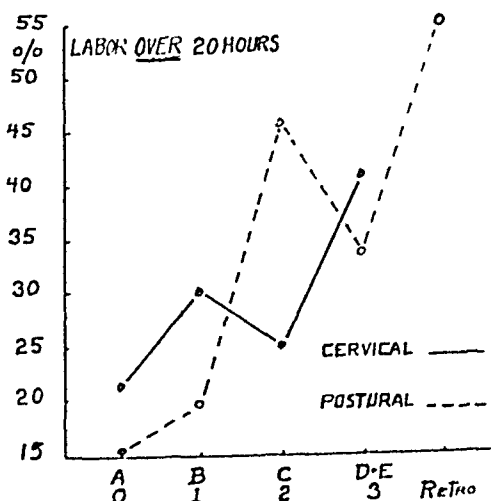


Fig. 3.

patients were old enough to be mature but young enough to retain the elasticity of their tissues.

RELATION OF THE DURATION OF LABOR TO CERVICAL INJURY AND MALPOSITION

The similarity of the two curves indicates that the duration of labor bears a definite relationship to the extent of damage incurred. In this group the ideal duration of labor was fifteen to twenty hours.

The reported incidence of malposition in primiparous women also shows wide variation. Reporting only second or third degree retroversions, Aldridge found 16 to 25 per cent; Peckham, 18 per cent; W. M. Findley, 26 per cent; Polak, 28 per cent; and Plass and Fullerton, 30 per cent. In our series there was an incidence of 28.5 per cent, six weeks postpartum.

With these facts in mind the chiefs of staff of the Philadelphia Lying-In Hospital laid down the following regulations for the postpartum care of all patients:

1. All patients were encouraged to lie on the abdomen for several hours daily during their hospital stay.
2. All patients were subjected to pelvic examination at the time of discharge from the hospital and malposed uteri replaced manually at that time.
3. All patients were advised to assume the knee-chest position (after instruction by a nurse) for ten minutes twice daily, to lie on the abdomen for one-half hour afterward, and to sleep in the prone position when at home. These were all ward patients in many of whom economic and social conditions made an immediate return to work imperative. Lynch's study of 1,230 cases showed that 44 per cent of ward cases showed a retroversion as opposed to 19.6 per cent of private patients and attributed this vast difference to economic conditions.

TABLE II. INCIDENCE OF MALPOSITION

CHARACTER	GRADE	NO. CASES	PERCENTAGE
None	0	103	53.4
First degree	1	24	12.4
Retrocessed	Retro	11	5.7
Satisfactory			71.5
Second degree	2	38	19.7
Third degree	3	17	8.8
Unsatisfactory			28.5
Totals		193	100.0

Because they were not considered as pathologic entities traceable to labor, first degree retroversions and retrocessions have been classified as satisfactory results; second and third degree retroversions are unsatisfactory.

TABLE III. INCIDENCE OF ADNEXAL DISEASE

TYPE	CASES	PERCENTAGE
Inflammatory	2 (G. C.)	1.0
Neoplastic	1 (Ov. cyst)	1.5
Postural	10	5.0

These statistics are presented only for their negative value. With the possible exception of the prolapsed ovaries no injuries to the adnexa could be attributed to the effects of childbirth.

TABLE IV. RELATION OF TYPE OF FORCEPS DELIVERY TO CERVICAL INJURY AND MALPOSITION

	COMPLICATED	LOW
Satisfactory cervix	69.7%	77.7%
Satisfactory posture	63.6%	66.7%

In general, it appears that the percentage of morbidity is proportional to the degree of injury sustained. The high percentage of morbidity among patients with normally posed uteri is striking. Analysis of the cases of morbidity in this group shows one-third due to pyelitis (following a grip epidemic), one-third due to breast engorgement, and inflamed perineum following repair, and one-third due to sapremia and endometritis.

TABLE VI. RELATION OF MALPOSITION TO SUBINVOLUTION

	MALPOSED	NORMAL
No cases	90	103
Subinvolved	17	4
Percentage	20%	4%

Subinvolution was 5 times as great among the malposed as among the normally posed uteri.

TABLE VII. RELATION OF MALPOSITION AND SUBINVOLUTION TO SAPREMIA AND ENDOMETRITIS

TYPE	CASES MORBID	SAPREMIA AND ENDOMETRITIS	PERCENTAGE
Normal	25	13	52.0
Malposed	18	12	66.6
Subinvolved	5	5	100.0
Totals	48	30	62.5

Sapremia and endometritis were roughly one and one-half times as frequent in the patients with malposition and two times as frequent in the patients with subinvolution.

SUMMARY

1. The lesions of the internal genitalia found at follow-up examination six weeks postpartum in 193 ward primiparas delivered by forceps at term are tabulated.

2. An incidence of 48.7 per cent of cervical lacerations, and 28.5 per cent of second and third degree retroversions is reported.

3. In the patients studied the group whose labor was between fifteen and twenty hours' duration showed the best results.

4. In the patients studied the group whose age ranged between twenty-five and twenty-nine showed the best results.

5. It is shown that patients delivered by low forceps operation show a higher percentage of satisfactory cervical results than those in which complicated forceps deliveries were done. It is suggested that the type of forceps delivery has little if anything to do with the incidence of malposition.

6. It is shown that poor anatomic results occur in patients with too rapid a labor as well as in those with prolonged labor.

7. It is shown that prolonged labor with its attendant malpositions may be due to a normal uterus, working against abnormal resistance to delivery or to a deficient uterus working against a normal resistance.

Short, violent labors produce cervical injury because sufficient time is not allowed for uniform dilatation, and the cervix is, therefore, more subject to laceration. In general, long labors show a higher incidence of laceration because of cervical dystocia, congenital and acquired, disproportion with large babies, and the higher incidence of complex operative procedures to terminate the prolonged labor. The apparent inconsistency of cervical results after twenty-five hours of labor is due to the retrocessed uteri in which we found 91 per cent satisfactory cervical results despite 55 per cent of labors above twenty hours.

Short, violent labors also damage the fundus. It is inconceivable to me that a uterus, capable of expelling a full-term fetus in less than ten hours, does not have good musculature before delivery. Therefore, the incidence of malposition after these labors must be due to actual damage incurred during labor. The malposition following long labor may be due to poor uterine musculature present before delivery or to damage incurred to a true dystocia due to any of the common causes. Fig. 3 will throw additional light on this problem.

RELATION OF CERVICAL INJURY AND MALPOSITION TO THE DURATION OF LABOR

It has been shown that in these patients the ideal duration of labor was fifteen to twenty hours. For this reason we have based this chart on the percentage of labors over twenty hours' duration.

In general, it would appear that the severity of the damage incurred varies directly as the percentage of labor above twenty hours.

Grade C presents an apparent inconsistency. This type of lesion most commonly follows short, violent labors so that 50 per cent of patients with Grade C lacerations have a duration of labor of less than ten hours. This accounts for the depression of the curve at this point.

Second and third degree retroversion also show an apparent inconsistency. The statistics represent the record of two widely different types of labor. In those patients with second degree retroversion 32 per cent had less than ten hours' labor and 35 per cent showed over thirty hours of labor. In those patients with third degree retroversion 44 per cent showed a labor less than ten hours and 28 per cent over thirty hours' duration. These percentages should present a fairly good index of the percentage of malposition due to too rapid labor as compared to the percentage associated with prolonged labor. As an index that both deficient uterine musculature and true dystocia play a part in the incidence of prolonged labor the study of retrocession has been listed separately. It is seen that the known deficient musculature was responsible for by far the highest percentage of prolonged labor.

TABLE V. RELATION OF CERVICAL INJURY AND MALPOSITION TO MORBIDITY

Cervix	Grade A	14.0%
	All others	29.0%
Posture	0	23.0%
	1	12.5%
	Retro	18.0%
	2	16.0%
	3	29.0%

bladder and then lifting a baby. A great factor in helping those patients keep the uterus in position is the advice to keep the bladder empty when working. The condition of the uterine wall depends upon the physique of the woman. Forceps delivery has less part to play in this subject than oversized children, producing extreme dilatation of the supporting ring at the brim of the pelvis. High forceps through an undilated cervix may, of course, produce the same results.

DR. JOHN McGLINN.—If we give the patients time to dilate the cervix, it is a rare thing to see a lacerated and traumatized cervix. If, on the other hand, you cannot wait to have the patient dilate the cervix satisfactorily, then you see the lacerations. If you are patient enough to let the patient have her baby in her own time, lacerations will not often occur.

DR. NUGENT (closing).—An examination two weeks after discharge from the hospital is of material value in detecting and instituting treatment in that large group of patients who leave the hospital with normally placed uteri, only to return with a retroversion at the sixth week following discharge.

Foulkrod's experience that heavy babies are followed by a high incidence of malposition supports Mengert's experimental work. He found that malposition was due in large part to injuries of the lower third of the parametrium and the upper third of the paravaginal tissues, rather than of the round ligaments, as was formerly thought.

SUPRARENAL CORTEX THERAPY IN THE VOMITING OF PREGNANCY

II. THE RESULTS IN SEVENTY-EIGHT CASES

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IN A previous communication¹ we presented the case report of a patient who had pernicious vomiting during pregnancy and who was apparently cured by the administration of suprarenal cortex. The rationale of this treatment, based upon Kemp's hypothesis² of the function of the adrenal cortex in the pregnant woman, was elucidated in that paper. Since then, we have prescribed the hormone in 78 consecutive cases of women in whom nausea or vomiting during pregnancy was a conspicuous symptom.

The hormone was dispensed in tablets and ampules, equivalent apiece to 3 gr. of dried adrenal cortex. The tablets were taken orally, while the ampules, containing 1 c.c. of solution, were administered either intramuscularly or intravenously. Hormone therapy was resorted to only after the ordinarily accepted remedies, such as alkalis, fruit juices, hypodermoclyses, and the like, failed to give relief. It must be emphasized that only the Armour product was used.

8. It is shown that there is a definite relation between poor anatomical results and the percentage of morbidity.

9. It is shown that subinvolution was five times as great among the patients with malposed uteri as opposed to those with normally posed uteri.

10. It is shown that sapremia and endometritis are one and one-half times as frequent in patients with malposed uteri and two times as frequent in patients with subinvolved uteri as in those who show neither of these conditions.

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DISCUSSION

DR. BEHNEY.—Many of us have sensed the relationship between lacerations, retroversions, subinvolutions of the uterus and benign uterine hemorrhage. Nugent's study justifies such opinions and will attract attention to an important feature of obstetrics and postpartum care.

DR. COLLIN FOULKROD.—I doubt very much whether we shall know much of this subject until someone is astute enough to have records of the uteri before the women become pregnant, to be compared with records of the uteri after labor. We do not know how many women have anteflexed uteri before delivery, so it is very difficult to say if retroversion is a pathologic condition in any way related to labor. I do not believe you can blame forceps delivery for retroversion, except that it may cause some trauma below.

On a first postnatal visit, we may find a uterus in good position, but six months later find it well back. I have seen uteri thrown back by a patient keeping a full

Group I: Nausea but no vomiting.—Only 6, or 7.7 per cent, of the patients belonged in this group. Four of them were experiencing their first pregnancy, and all were in the first trimester of their present one. Their ages ranged from twenty-three to thirty-six years and their weights from 100 to 198 pounds. In addition to being nauseated they felt slightly weakened; not one, however, showed any signs of ketosis. They were given the tablets only.

Five of the group were entirely relieved of nausea in from one to two weeks; of these, 3 were relieved within the first week. The sixth patient reported that no relief was obtained, but she eventually ceased to be bothered by the nausea when her second trimester was reached.

Group II: Moderate to Severe Nausea and Slight to Moderate Vomiting.—Forty-one, or 53 per cent, of the treated patients were included in this group. Their ages ranged from twenty to thirty-eight years, and their weights between 113 and 204 pounds. All were in the first trimester of their present pregnancy, and the majority of them had had one or more previous pregnancies. All had a marked weakness in addition to nausea and vomiting. Thirty-nine had no ketosis; the remaining two had only slight acetoneuria. Forty patients were given the tablets alone, and one patient had an initial course of intramuscular injections. The entire group was treated at home.

Of the 40 patients who were treated with the tablets only, 39 were entirely relieved within one to two weeks, while the remaining patient obtained no relief whatsoever. She was lost trace of soon after and no further medication or study was possible. The only member of the group who received the hormone intramuscularly was entirely relieved of all symptoms by the end of the second day.

Group III: Severe Nausea and Severe Vomiting.—This group numbered 15, or 19 per cent of the patients studied. Their ages ranged from twenty-one to thirty-four years and their weights from 124 to 173 pounds. Only one patient was a primipara. All but 2 patients were in the first trimester of their present pregnancy, while the remaining 2 were in their second trimester. All of them felt a marked weakness in addition to the nausea and vomiting. Their urine contained only traces of acetone; there was no diacetic acid. Even though all the patients were treated at home, they were given the hormone initially via the hypodermic route.

All the members of the group were completely relieved of their symptoms within three to five days following the beginning of the therapy, while most of them felt markedly relieved within the first twenty-four hours.

Group IV: Pernicious Vomiting.—Belonging to this group were all the patients who vomited everything taken by mouth and whose urine contained large amounts of ketone bodies. Sixteen, or 22 per cent of the entire number, belonged to this group in which is included the patient whose case we had reported previously.¹ The majority were in their first trimester of their present pregnancy and were multiparas, while the remainder were in the second trimester and were primiparas. Their ages ranged from twenty-five to thirty-six years and their weights from 133 to 190 pounds. They had previously been treated at home with about every known medicine used for this condition, but without obtaining the slightest relief. All of them had to be sent to the hospital where they were given glucose-saline solution intravenously immediately. The hormone was administered later by the same route.

Fifteen of the group became symptom-free by the fifth day following the beginning of the treatment and the majority of them by the third day. Every one of them reported that they felt much improved within the first thirty-six hours. The remaining patient of this group presented such unusual and interesting features as to warrant a more detailed story.

The tablets were given to those who were merely nauseated or who vomited but rarely or at regular intervals. With these patients we were reasonably sure that the tablets would not be vomited. All members of this group were ambulatory and were self-administrators of the drug. They were told to take one tablet three times daily, about one-half hour before their regular meal. If at the end of a week their symptoms had not completely ceased, the dose was increased up to six tablets a day. The use of the tablets was continued until the entire contents of a bottle of 100 were taken. In only one instance was it found necessary to prescribe more than one bottle for any patient.

The hypodermic route was prescribed for those patients who vomited at irregular intervals or who vomited everything taken by mouth. The contents of one ampule (1 c.c.) were injected three times a day, about one-half hour before the regular mealtime. The injections were continued thus for three days *after* the disappearance of all signs of vomiting; then one ampule was replaced by one tablet on each successive day, so that by the end of the sixth day after cessation of vomiting, the patient was receiving three tablets a day and no ampules. The use of the tablets was then continued until 100 had been taken. Ambulatory patients were given the injections by the district nurse, relatives, or friends, or even took them themselves.

RESULTS

For clarity of description we have divided the group of 78 patients into subgroups bearing reference to the severity of the symptoms. The results are summarized in the accompanying table.

TABLE I

TYPE OF CASE	NO. OF CASES	AGE RANGE	PARA RANGE	TRIMESTER	WEAKNESS	KETOSIS	CORTEX R	EFFECT
I Nausea alone, no vomiting	6	23 to 36	i to ii	First	Moderate	0	Tablets only	5 cured (1-2 weeks) 1 failure
II Moderate to severe nausea and slight to moderate vomiting	41	20 to 38	i to v	First	Marked	None 39 Slight 2	40—Tablets alone 1—Ampules	40 cured 1 failure Ampule cured
III Severe nausea and severe vomiting	15	21 to 34	i to iv	First and second	Marked	Slight	Ampules replaced by tablets	All cured in 1 to 5 days
IV Pernicious vomiting	16	25 to 36	i to iv	First and second	Marked	Marked	Ampules replaced by tablets	15 cured (3-5 days) 1 only after vitamin therapy

DISCUSSION

Kemp's hypothesis was formulated through the postmortem study of the adrenals of only a few women who died of trauma during the pregnant state. It is evident, therefore, that our therapeutic study must be considered as purely empirical, and that many more patients must be studied and a suitable number set up as controls before a fair evaluation can be made. This is a problem for future work. Our present discussion will be adjusted to the requirements of an adequate but conservative estimate of the results obtained.

It is evident that the age, weight, and multiparity of the patient bear no relation to the severity of nausea, vomiting, and weakness. It is likewise evident that the age, weight, and multiparity of the patient bear no relation to the effect obtained by the suprarenal cortex medication.

The psychic factor, which is so notably present in pregnant women, is difficult to evaluate at present. It must be remembered, however, that in all instances the suprarenal cortex was not used until after the patient failed to get any relief from the medicaments ordinarily used. To the patients, then, the suprarenal cortex was just another drug and, as such, could not have been a more potent psychic stimulus than the other drugs. To those patients who received the medication hypodermically, it may be supposed that the needle injections alone may have been of sufficient psychic stimulation to cause their vomiting to stop. All of the patients were given glucose-saline parenterally quite a few hours before the hormone was given, and in our first case the patient had been given glucose-saline intravenously for several days before the suprarenal cortex administration was started. In no instance did the nausea or vomiting lessen because of the use of the needle before the adrenal cortex injections. It is evident, therefore, that no matter how important the psychic element may have been, it was not the all-important factor.

Muscular weakness was an accompanying symptom of nausea and vomiting in almost every patient, the severity of weakness being in direct proportion to the severity of the nausea and vomiting. The single exception was that of a patient who developed a rather typical syndrome of peripheral polyneuritis.

Because in the first group there were but six cases, which is too small a number for analysis, and because the symptoms of the patients of the second group were similar in character to the symptoms of the patients in the first group, only a bit more severe, the two groups may be discussed as one. That they are similar in character is evident by the presence of nausea, weakness, and the lack of a definite ketosis. The dissimilarity is in the degree of vomiting, which in no instance was severe.

CASE REPORT

Mrs. M. was thirty-three years of age and was in her second pregnancy; she had been delivered of twins at her first pregnancy, when she was twenty-six years of age. The twins had been delivered without too much difficulty and their subsequent development had been uneventful. While she was in the first trimester of her present pregnancy, she had vomited considerably at irregular intervals and had been given the usual alkalies and fruit juices, as well as thyroid tablets for she was slightly obese. Soon after, because her vomiting had become more severe and because traces of acetone were found in her urine, she was sent to the hospital and was given glucose-saline and suprarenal cortex intravenously. Her symptoms ceased before the third day. On the third day she felt so markedly improved that she asked to be allowed to go home. Contrary to our better judgment she went home, but the necessity of faithfully taking the suprarenal cortex tablets was impressed upon her. Two weeks later she returned in a condition similar to that of her former admission. Again her symptoms cleared readily with the intravenous hormone therapy, and again she pleaded to go home on the third day. This time her husband joined in on the request. She went home against advice but, as before, instructions were given her concerning her treatment.

About a month later she reported once more in a state of dehydration and ketosis, but this time it was much more severe. At home, she had tried all kinds of remedies, of her own accord, upon the advice of relatives, friends, and neighbors. Her symptoms had not only persisted but had actually become worse; she was so weak that she could not walk even with assistance. She had hesitated to report to her physician because she hoped that the vomiting would stop when she entered her second trimester, and because of the hospital expense.

At the hospital her urine was found to contain large amounts of both acetone and diacetic acid. Moreover, her mind began to wander. It was apparently difficult for her to concentrate, for she answered questions slowly, in a hesitating manner. She was often irrelevant and her memory for remote and recent events was impaired even as to her own age and the ages of her husband and children. Within three days after entry into the hospital, she began to tolerate food in her stomach, but her strength and memory were failing; she could not recognize her husband and children part of the time. Her urine had lost all traces of diacetic acid, but because it was not acetone-free, and despite the fact that her blood sugar was only 83 mg., she was given five units of insulin three times a day, together with the glucose saline and hormone. Her urine became acetone-free within twenty-four hours and she ceased vomiting entirely. Her strength and mental condition, however, appeared to be worse than ever. She also complained, at this time, of pains in both lower legs. A few nights later, the nurse found her lying on the floor near the bed. At the time, she related to the nurse that she attempted to go to the bathroom but that her legs would not support her when she stood up. The following morning, in answer to direct questioning, she could not remember falling to the floor and neither could she remember attempting to get out of bed. A complete neurologic examination revealed that she had a peripheral polyneuritis. Large doses of vitamin concentrates were added to her diet. Within a few days the pains in her legs completely disappeared and her strength gradually returned. By the end of the week, she had regained so much of her strength as to be able to walk without assistance; her mental condition, too, was better. She was then allowed home in the care of her mother. At home, with the same vigorous dietary regime, she recovered completely except for a slight, left leg-lag which was noticeable only on careful scrutiny. At the end of her full-term pregnancy, more than four months ago, she was delivered without much difficulty of a normal and healthy baby.

It is unlikely that in the few instances that insulin was given, it acted any more than as an adjunct to the quicker recovery of the patient. Insulin was administered only to those patients whose ketosis did not clear as rapidly as vomiting and was never given early in the course of treatment. It was most peculiar, though, that of every patient who received insulin, their blood sugars were all in the low eighties before the first insulin injections. A satisfactory explanation for this phenomenon has not yet been advanced.

It is probable that in a study of an adequately controlled and larger group, the number of failures with the suprarenal cortex therapy will be increased and more nearly approach the proportion of failures with other therapeutic regimes. This, however, can be stated: even if a larger percentage of failures may occur, for the present suprarenal cortex therapy not only is the easiest regime so far advanced but, also, it actually reduces the expenses of hospitalization for the patient, and reduces the expenses of the hospital itself. There are no long, tedious and expensive tasks to this therapy.

Up to the present, no contraindications have been encountered with the use of this drug in pregnant women who are suffering with nausea and vomiting.

It is a well-known fact that different endocrine manufacturers use different methods for extracting some of the endocrine glands. It is also well known that variations in the methods of extraction may not only vary the potency of the resulting hormone, but may even yield an entirely different hormone (or hormones) having absolutely different effects in the human body. In our first case we used Armour's preparation at Kemp's suggestion, and since we wanted to study the efficacy of the drug, it was necessary to use a product similarly extracted. For these reasons we used the Armour product exclusively. We have no idea what effects, if any, would be obtained by using adrenal cortex extracts manufactured by others. It is with these considerations in mind, and not because of any other interest, that we emphasize the use of the Armour preparation in order to get comparable results.

SUMMARY

Seventy-eight pregnant women were treated for nausea and vomiting with Armour's suprarenal cortex after the failure of the ordinarily used remedies for this condition. The less severe cases of nausea and vomiting were treated exclusively with tablets; the more severe cases were treated at first with parenteral injections of the hormone.

Of the 47 treated patients with less severe nausea and vomiting, only two, or 4.3 per cent, failed to receive any benefit from the hormone.

With the combination of Groups I and II, there were 47 treated patients of whom 2, or 4.3 per cent, were definite failures. Only one patient was given an initial course of the medication via the hypodermic route, and she was readily cured. It is to be noted that the patients successfully treated with the tablets alone, 44 in number, required from one to two weeks' medication before the symptoms had entirely disappeared, although many of them felt much relieved before this time.

In Group III, 15 cases constituted the series. The medication was given hypodermically in every instance, and a cure was effected in every case within from three to five days. The patients in Group III were much sicker than the patients in Groups I and II, yet they were cured in about one-third the time. We should expect that any drug taken orally by pregnant women would reveal its effects more slowly and with more of an uncertainty than if given parenterally. The self-administration of any drug by the patient is a method always full of uncertainties and uncontrollable factors. It is dependent upon the faithfulness of the patient, the motility and the absorptive action of the gastrointestinal tract. Pregnant women are noteworthy for their sluggish gastrointestinal tracts. It is reasonable to conclude, therefore, that if the discomfort and severity of nausea and vomiting are serious enough to warrant treatment, the medication should be given in a manner to yield the quickest and most reliable results.

In the fourth group (IV), that of pernicious vomiting, there were 16 patients treated. It must be reemphasized that, in every instance, these patients had been treated with almost every kind of remedy at home before they were put on suprarenal cortex medication. No material benefit was observed by the preliminary liter of glucose-saline injected intravenously upon their admission to the hospital. It is true that not much time was allowed to elapse, only a few hours, between the initial glucose-saline and the first dose of adrenal cortex solution, except in the first case when the patient had received injections of glucose-saline for days before the hormone therapy was started. After the first case, we did not feel it safe or fair to the patient to allow too much delay for experimentation.

It was the study of Mrs. M.'s case, whose report is quoted in detail, that taught us the value of vitamin concentrates in the patients' diets. Thereafter, all subsequent patients were given high vitamin, fat-free diets to begin with, as soon as they could tolerate food. Gradually a regular diet, rich in vitamins, was given as the progress of the patient warranted. Too much stress cannot be laid upon the necessity of rapid vitamin replacement in the body. It must be remembered that protracted vomiting not only leads to dehydration and ketosis but also to avitaminosis, and all three conditions are serious and must be treated with equal vigor. Avitaminosis may not only lead to serious complications but, if prolonged, it may even lead to death itself.

studied, showed a space of from 1 to 2.5 cm. between the fetal head and bladder. However, in this series the technic used was quite different. Intravenous injections of skiodan (20 c.c.) were given, after which the x-ray films were made.

We have followed a series of cases at Saint Mary's Hospital and have found that x-ray studies in cases of uterine hemorrhage occurring in the last trimester of pregnancy assume a great importance both as adjuncts to clinical diagnosis and as guides to choice of treatment. Proper interpretation of information afforded by these studies should lessen greatly the existing chance of instituting improper treatment and also do much to eliminate trial-and-error methods.

A digital examination, although of final importance in the differentiation of uterine bleeding, incurs the possibility of immediate delivery when such procedure might be disadvantageous to mother and child alike. It also incurs the danger of contamination of the birth canal with subsequent infection, which danger is second only to that of renewal of hemorrhage. At this point, x-ray films have proved extremely valuable in locating the placenta. We used the technic described by Ude and Urner. A number of such cases were followed with confirmation of x-ray and clinical diagnosis in all cases, except one of ablatio placentae, in which the film showed the same variation in relation of fetal head to bladder as found in placenta previa centralis. In this case, however, the clinical diagnosis of ablatio placentae had been made and the change in relation between fetal head and maternal bladder was ascribed to a bulge of fore-water caused by the markedly tense uterus or by concealed hemorrhage and blood clot. An appreciable space existed between presenting part and bladder, but there was no bladder deformity resembling that which was seen in the placenta previa cases.

Of 40 cases of bleeding, 18 were cases without placenta previa. Seven were placenta previa, five were breech presentations, and the remainder were normal controls of seven, eight, and nine months' gestation.

The points considered in estimating the position of the placenta in our series were as follows:

1. During the last trimester, the presenting part lies in close apposition with the bladder, being separated by only a few millimeters of lower segment, scalp, and bladder wall. (Throughout this discussion we are concerned principally with cephalic presentations, as in breech presentation x-ray is of only speculative value and in transverse presentation of no value at all.)

2. The intervention of a soft tissue mass, such as placenta, produces an alteration in this relation in the form of an appreciable space, which we believe must approach 1.5 to 2 cm. to be of importance.

3. The apposition causes a concavity to appear in the superior wall of the bladder which corresponds to the convexity of the presenting part and which lies in the plane of transmitted pressure.

There were 15 patients who had severe nausea and vomiting and 16 patients who were classed as having pernicious vomiting. A cure was effected in every instance within from three to five days with the parenteral treatment. It is important to note that in no instance did the condition of nausea and vomiting become more severe, necessitating the interruption of pregnancy.

In the more severe cases of nausea and vomiting, the body fluids and vitamins were replaced as rapidly as possible. In those patients in whom the ketosis did not clear as rapidly as their clinical symptoms, insulin was added to their intravenous medication.

The lack of an adequately controlled study has been discussed.

No contraindications of the use of suprarenal cortex have been encountered.

CONCLUSIONS

Suprarenal cortex is an efficacious and important therapeutic weapon in combating the various types of vomiting due to pregnancy. As used by us, it is a more reliable and less costly therapeutic regime than any tried heretofore. Our results warrant its use as well as further study in combating the condition.

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THE DIAGNOSTIC VALUE OF THE X-RAY IN PLACENTA PREVIA*

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OUR interest in the x-ray diagnosis of placenta previa was aroused by a paper of Ude and Urner,¹ who reported a series of thirty-five cases with bleeding in the last trimester of pregnancy, of which fourteen were placenta previa, diagnosed by x-ray. Their technic included the instillation of 40 c.c. of 12 per cent sodium iodide in the bladder, followed by a direct anteroposterior x-ray of the abdomen. Diagnosis of placenta previa was made on finding a space between the presenting part and bladder of more than 1 cm.

Our interest was further aroused by an article by Hundley, Walton, Hibbitts, Siegel and Brock² in which ten of twenty-seven normal cases

*Read before the Brooklyn Gynecological Society, April 3, 1936.

CASE 2.—Forty-four-year-old white gravida xiv, para vi, admitted during the eighth month of pregnancy, with history of intermittent bleeding of small amounts during past two months. During the two days before admission, she had slight cramplike abdominal pain at irregular intervals. On morning of admission, however, patient was awakened by profuse painless vaginal bleeding. The clinical diagnosis made was that of placenta previa. X-ray showed the bladder to be displaced to the left with the maximum of soft tissue space just to the right of the midline. X-ray diagnosis was partial placenta previa with the bulk of placenta lying to the right of the os. This was confirmed at the time of rupture of membranes and version. The x-ray diagnosis of partial placenta previa thus gave us from the beginning a clearer idea as to the pathology present and made the choice of vaginal delivery much easier.

CASE 3.—Twenty-seven-year-old colored gravida iv, para 0, admitted in the seventh month of pregnancy, with history of having awakened four hours prior to



Fig. 3.—Case 3. Ablatio placentae showing appreciable space between fetal head and maternal bladder but lacking characteristic flattened appearance of bladder seen in placenta previa cases.

admission with severe cramplike pain in the lower abdomen, which was followed by a steady moderate flow of blood from the vagina. Pain and bleeding continued throughout time of observation. Uterus was tense and felt larger than a seven months' pregnancy. A clinical diagnosis of ablatio placentae was made. On x-ray examination, there was found an appreciable space between the presenting part and the bladder. The form of the cystogram in this case showed only a very slight departure from that of the normal cystogram seen in nonpregnant subjects. It was directly comparable to that seen in early pregnancy and also in a case of transverse presentation, in which case insufficient pressure was exerted on the bladder to cause any notable deformity. Patient was prepared for delivery and for transfusion and a vaginal examination was done. The membranes were ruptured, a Voorhees' bag No. 4 inserted and the patient allowed to deliver normally. No placenta was felt near the os. The placenta, after delivery, showed a large darkened central area compatible with ablatio placentae. This case brings out the

Therefore, from this it is possible to determine not only the presence of placenta but also to estimate its position as shown by the plane of bladder deformity.

The following cases illustrate the above points:

CASE 1.—Thirty-six-year-old white primipara admitted during eighth month of pregnancy, with history of painless bleeding. Patient said she had an uneventful



Fig. 1.—Case 1. Central placenta previa showing space between fetal head and maternal bladder with bulk of placenta lying at left of midline. Diagnosis confirmed at cesarean section.

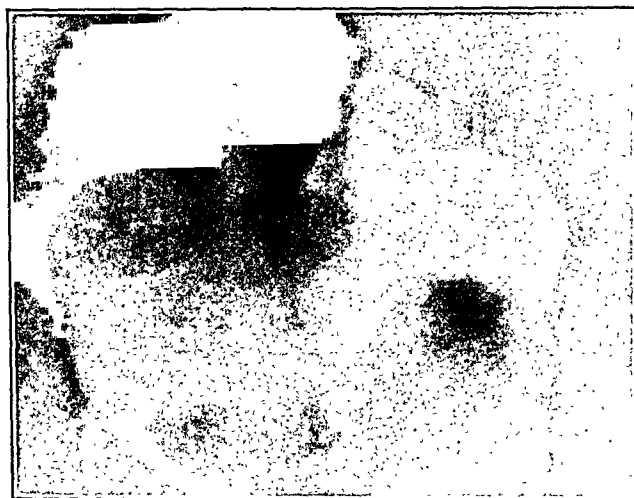


Fig. 2.—Case 2. Partial placenta previa with head displaced to right and bladder to left. Placenta found on left side at time of version and extraction.

pregnancy up to twelve hours before admission, when she bled about 300 c.c. without apparent cause. X-ray revealed central placenta previa with widest part of placenta just to the left of midline of pelvis. Patient carried to term with conservative treatment, when she bled slightly and cesarean section was done with good result. Central placenta previa as diagnosed by x-ray was found.

The position of the placenta, as estimated by the plane in which pressure was apparently transmitted to the bladder wall, was confirmed at operation.

The value of x-ray in breech presentations is doubtful. However, we were fortunate in securing films of such presentations, both normal, at seven, eight, and nine months and also of a breech presentation complicated by placenta previa in the eighth month. The three normal cases showed the breech in close apposition with the bladder, while that of the placenta previa, although the film was considered unsatisfactory, did reveal a large space between the presenting part and bladder.

CASE 5.—In our series only one patient with low implantation of the placenta was x-rayed. This was a thirty-seven-year-old white gravida iii, para i, who was admitted during the seventh month of pregnancy. Her history was that of painless bleeding without cause. The films showed the presenting part in apposition with the bladder. She was treated expectantly and delivered during the eighth month, at which time a diagnosis of low implantation was established. Eighteen cases with painless, causeless bleeding during the last trimester, which were x-rayed, showed no appreciable space between the head and bladder wall. These patients subsequently delivered normally. The clinical diagnosis in these cases was not definite, and placenta previa could not be ruled out without x-ray, or a vaginal examination with possible contamination of the birth canal and hemorrhage.

From the above observations we conclude that x-ray in cases with bleeding in the last trimester of pregnancy is of value as an adjunct to the clinical diagnosis and as an aid in locating the placenta in central or partial placenta previa.

We believe that a diagnosis of placenta previa, central or partial, can be definitely ruled out in bleeding cases in the last trimester of pregnancy, which, when x-rayed, show no appreciable space between the presenting part and the bladder.

A bleeding case in the last trimester, which when x-rayed, shows a definite space between the head and bladder, may be placenta previa. If this space is accompanied by a marked bladder deformity, placenta previa is very probably present. Only a most careful digital examination should be made in an attempt at confirmation, and this only when all preparations for delivery, in the manner suggested by x-ray and clinical findings, have been made.

A choice of procedure, if clinical diagnosis confirms x-ray findings, can be more scientifically determined because of the aid in locating the placenta afforded by x-ray.

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34 PROSPECT PARK, W.
220 MAIN STREET

DISCUSSION

DR. FRANK P. LIGHT.—On Dr. Beck's service at Long Island and on Dr. Duncan's service at the Kings County Hospital we have been taking these pictures over a period of three years. During that time we have had a series of 60 such

point that an appreciable space between the presenting part and bladder does not always mean placenta previa. An alteration in the form of the cystogram suggesting transmitted pressure must be watched for, and the clinical findings should be used in conjunction with those of the x-ray for a correct diagnosis in such cases.

CASE 4.—Thirty-five-year-old colored gravida ii, para 0, admitted in the eighth month of pregnancy from our clinic because of inability to hear the fetal heart.

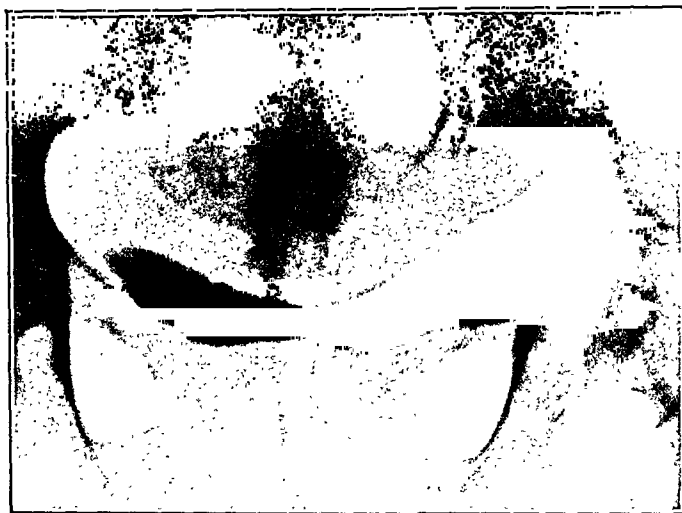


Fig. 4.—Case 4. Central placenta previa diagnosed by x-ray and confirmed at delivery.



Fig. 5.—Case 5. A bleeding case with no space between fetal head and maternal bladder. This resembles the cystograms of normal cases in the last trimester of pregnancy. At time of delivery no evidence of placenta previa was found. This confirmed the x-ray diagnosis.

Previous pregnancy terminated in a stillbirth at term. No history of bleeding or any other abnormality during present pregnancy. An x-ray study made to determine presence or absence of postmortem fetal changes showed presence of a central placenta previa. No fetal heart was obtained up to time of delivery, when x-ray diagnosis of central placenta previa was confirmed.

in a nonpregnant state. The condition is more or less transient, but may recur at intervals and persists not longer than ten to twelve days. Either the anterior lip or entire cervix may be involved. The etiology is obscure but it is probably angioneurotic.

Mrs. B., aged twenty-nine years, para ii. Patient was first seen at end of second month. Examination at this time revealed no pathology. Past history was negative. Pregnancy progressed normally until early in the seventh month, when by telephone she reported a "swelling in the vagina." When seen there was a purplish mass protruding from the vagina the size of a small orange, from which exuded a moderate serosanguineous discharge. This proved to be an enormously swollen and edematous cervix which pitted on pressure, and could not easily be replaced within the vagina. It was thought at first that the condition was that of a prolapse with the attendant edema due to pregnancy. However, on bed rest, and with wet dressings, the edema completely subsided during the following eight days and it did not recur during the remainder of the pregnancy. Labor was easy and uneventful. No prolapse could be demonstrated postpartum and there was no residual pathology in the cervix other than a mild cervicitis.

II. *Acute Edema of Cervix Occurring During Labor.*—Acute edema of the cervix occurring during labor, while apparently a rare condition if the volume of published cases is a criterion, undoubtedly occurs more frequently than we have been taught to expect. It is possible that the reason for its unusually rare appearance in the literature is due in part to the fact that most "classifications of diseases," such for instance as that of Massachusetts General Hospital, make no mention of the condition as a complication of pregnancy or labor, and consequently these cases as such do not appear in the hospital files. In our own experience we can vouch for the accuracy of this observation, as it has been difficult to collect the twenty cases herein reported, although in consulting individual obstetricians, the condition for the most part is well recognized. We were able to find twenty cases in 12,461 deliveries, an incidence of one in 623. Cathola and Seydel report one in 448 deliveries.

It may be well to state at the outset that in our opinion the etiologic factors concerned in the production of this type of edema of the cervix are not the same as those concerned in edema occurring during pregnancy, namely, the angioneurotic type. In fact, we believe that there may be several factors and combinations of factors concerned in the production of this condition.

The interest to the practicing obstetrician in this group of cases lies mainly in its effect upon the course of labor. Labor progresses to various degrees of dilatation in the first stage depending upon the time that the edema occurs. From then on in spite of pains which are frequently stronger and of longer duration than usual, progress stops and there may be no advance in the course of labor for an indefinite period. If the condition is not recognized and treated, the patient may labor with gradual diminishing pain and with, eventually, signs of exhaustion. The formation of a contraction ring may even occur. At times a dis-

pictures, of which 12 were of cases with placenta previa. In most of our cases the x-ray diagnosis was confirmed by the subsequent clinical findings, but in a few cases we found the plates misleading. Our final opinion must therefore be reserved until we can study a larger series of cases.

DR. CAMERON DUNCAN.—If you intend to perform a Braxton Hicks or even a typical version, the cystogram gives you a pretty good idea as to which side the placenta is chiefly located. You can use the side where the cystogram is the fullest, with more safety than the side of placenta. That information we found to be of considerable help.

DR. HALL (closing).—I feel that the x-ray is of special value in the eighth month of pregnancy where there has been a fairly brisk hemorrhage, and you are not sure whether you have a viable baby. The x-ray will save the necessity of a vaginal examination which might entail immediate delivery on account of hemorrhage.

ACUTE EDEMA OF THE CERVIX IN PREGNANCY AND LABOR

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AN EXAMINATION of the literature on edema of the cervix occurring during the pregnant state shows that practically all authors are reporting only one of what we consider to be two distinct conditions with different etiologic factors: in one the edema occurs during pregnancy (I), in the other during labor (II).

In 1872 Gueniot^{1, 2, 12} published the first report of acute edema of the cervix occurring during pregnancy. Since that time the literature has been remarkably sterile of reference to this condition. Jolly³ in 1904 was able to report 10 cases of edema of the cervix complicating pregnancy, including 8 cases previously reported by Geyl¹⁵ and 1 case seen by Meyer. Hunter⁹ states that it has been possible to collect reports of 30 cases published in the past fifty years (from 1927), and that of these, 24 occurred during pregnancy. To this group DeLee¹ has added 3 cases, and an additional case is reported in this paper.

We do not consider in the above classification edema of the cervix occurring as the result of prolapse of the pregnant cervix, since the etiology of the condition here is self-explanatory, and also because we do not believe the condition can be considered as one of acute edema.

The interest in Group I cases is largely in the rarity of the condition as evidenced by the scarcity of reported cases (28 inclusive).

Group II cases are of interest both on account of their comparative rarity, although in our opinion occur much more commonly than we could be led to expect, by a study of the literature, and on account of their influence on the course of labor.

I. Acute Edema of the Cervix Occurring During Pregnancy.—Acute edema of the cervix has been seen during the second, third, and seventh months, and also at the end of pregnancy, and undoubtedly may occur at any time during gestation. Jolly claims that it has never occurred

Age incidence is probably of some importance as an etiologic factor in primipara. Acute edema of the cervix apparently occurs rarely in young primiparas. The average age of the primiparas¹⁵ concerned in this group was 29.3 years (Table I). If the commonly held idea that elderly primiparas frequently have fibrous cervixes is correct, then we may have in these cases at times an "obstruction to the outflow of fluids" with the production of edema during labor. The same can be said for the edema occurring in multiparas; the trauma of previous labors, resulting in scar tissue formation, plus pressure of the presenting part against the cervix may at times result in edema.

In considering the effect of a contracted pelvis on labor, Irving⁶ says, "the anterior lip of a partially dilated cervix may be incarcerated between a tightly impacted fetal head, and posterior surface of the symphysis. In such an instance the anterior lip becomes edematous and further progress ceases. This condition is particularly likely to complicate a flat or rachitic pelvis." Cathola and Seydel⁷ also mention the frequency of its occurrence during the course of labor in cases with moderately contracted pelvis. The finding of edema of the cervix during labor in two of our cases, one with a flat pelvis, and one with a moderately generally contracted pelvis, both in primiparas, would seem to confirm the above observations.

The rôle of posterior positions cannot be overlooked in a consideration of etiology. Among the twenty cases under consideration, eight occurred in patients with posterior positions of the occiput.

TABLE II. POSITION

LOA	ROA	ROP	LOP	SLP
4	8	6	2	1 (twins)

We have not encountered face, brow, or transverse positions in our series, although edema of the cervix has been reported⁷ as occurring in these conditions.

Of great importance is the effect upon the duration of labor. It is generally recognized in the scanty literature, as has been mentioned before, that labor may be indefinitely and dangerously prolonged unless the cause of dystocia is promptly recognized and treated.

This observation we believe to be of particular importance where primiparas are concerned. The average length of labor in our cases was twenty-nine hours, which is far in excess of the time usually considered to be normal for primiparas. In the multiparas the lengthening of labor has not seemed to be so important. The average length of labor was 13.5 hours, which we do not consider to be excessive. This would seem to be explained, after analyzing the labors of the five multiparas concerned, in part by the fact that they seem to have been recognized and treated earlier than was the case in the majority of primiparas.

colored cystic appearing cervix may appear at the vulva, and be mistaken for the bag of waters. We have known of instances in which attempts at rupture have been made before the condition was recognized. Either the anterior lip or the entire cervix may be involved in this process; the former, however, is much more common. As the head descends into the pelvis, the anterior lip impinges behind the symphysis pubis and is compressed with each pain, which aggravates the condition already present. We have seen two cases of complete avulsion of the cervix resulting in neglected cases. In one the patient entered the hospital after many hours of labor, bringing with her a mass of cervical tissue, showing marked edema and dilatation of the external os to about 4 cm. In the second case, also long in labor before entrance, a mass of same character was removed from the vagina.

Early diagnosis is important both from the standpoint of the mother and the child, and if unrecognized, progress in labor may be delayed indefinitely. It is probable that in many cases recognition of the condition has not been made because reliance has been placed entirely upon rectal examination, and it is very easy to overlook a moderate edema of the anterior lip, which is most commonly encountered, unless vaginal examination is done.

Treatment will depend upon the condition when first discovered as the cause of dystocia. If the head is well down in the pelvis and the cervix well dilated, simply lifting the anterior lip over the impinging occiput and allowing labor to progress normally is all that is necessary. If delivery has been delayed until the patient is exhausted and uterine contractions no longer adequate, it may be necessary to terminate labor by operative means. If edema has occurred before there has been sufficient dilatation to allow passage of the fetal head, it may be necessary to do Duhrssen's incision and terminate labor operatively. We have not yet encountered a case occurring so early in the course of labor as to make the use of Duhrssen's incision dangerous; that is, cervical dilatation had progressed to 4 cm. or more. Should a case be encountered in which cervical dilatation and retraction of bladder, ureters, and pelvic vessels was not sufficient to make this procedure safe, we believe that vaginal hysterotomy followed by operative delivery from below would be the procedure of choice; particularly if the pelvis was normal.

Calhoun⁷ states that all cases observed by him were multiparous patients and therefore considered the edema due to previous trauma to the cervix. We do not agree that multiparity is the only etiologic factor, as among twenty cases fifteen of ours were primiparas.

TABLE I. PARITY AND AGE

Para i	15	Average age 29.3 years
Para ii :	2	} Average age 35.8 years
Para iii	1	
Para iv	1	
Para vi	1	

plicating factor in labor. Very little active treatment is required. It is probably angioneurotic in origin.

Acute edema of the cervix during labor results in serious dystocia more commonly than is usually supposed. The etiologic factors are multiple. Prompt recognition and treatment are imperative to avoid high fetal mortality and maternal morbidity.

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1807 DAVID WHITNEY BUILDING

THE INCIDENCE OF URETERAL STRICTURE IN LOWER ABDOMINAL PAIN IN WOMEN*

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INTEREST in ureteral stricture was first stimulated by Hunner, who, in 1916, reported a series of 50 patients with ureteral stricture and in 1918 a series embracing 100 patients. Following these two presentations, he wrote numerous papers on the various⁶⁻¹² aspects of ureteral stricture. Laws¹³ in 1926 presented a series of 50 patients among whom were 8 with stenosis, one with traumatic stricture, two with ureteral anomalies, and 18 with ureteral calculi.

Fetterman¹⁴ in 1932 reported a series of 1,164 patients of whom 471, or 41 per cent, were proved cases of referred ureteral pain. Stevens and Henderson¹⁵ in 1929 reported an incidence of 11.3 per cent of ureteral stricture among their urologic patients. In 1928 Ginsberg²² reported a short series of cases emphasizing abdominal symptoms. In 1927 Schreiber¹⁶ reported his findings in a series of 100 consecutive autopsies designed to determine the frequency of ureteral stricture and found a total incidence of 25 per cent (21 were children). However, in analyzing the 79 adult cases, he found that 25, or 31 per cent, had stricture. Frater and Braasch¹⁷ in 1929 examined 93 unselected cases (48 males, 35 females) at autopsy, removing both kidneys and ureters, but it is not clear whether or not that portion of ureter passing through the broad ligament had also been removed. No percentage was given but they stated that the incidence of lesions of the ureter was greater than had been previously recognized. In a series of 739 patients examined, Rathbun¹⁸ found 92 cases of stricture (12 per cent).

*Read at a meeting of the Obstetrical Society of Philadelphia, October 1, 1936.

TREATMENT

The treatment has consisted either in lifting the edematous cervix over the occiput and behind the symphysis followed either by spontaneous or operative delivery, or in Dührssen's incision followed by operative delivery.

TABLE III. TREATMENT

Cervix lifted over the occiput (5)	
Spontaneous (cervical dilatation 8 to 9 cm.)	3
Low forceps	1
Version, extraction (cervix lifted over after-coming head)	1
Dührssen's incisions of the cervix (15)	
Midforceps (cervical dilatation 3 to 7 cm.)	4
Version, extraction	11

Obviously the simplest method of treatment is to lift the cervix over the occiput and behind the symphysis, holding it in this position until a succeeding pain or two makes its prolapse impossible on account of the advance of the head. This is possible when the edema involves chiefly the anterior lip, and when dilatation is practically complete at the time that the condition is discovered, and when the patient's condition is still sufficiently good that labor will still progress.

There are encountered, however, cases in which this simple procedure is not applicable because dilatation of the cervix is not sufficient to make it possible. In most instances we have found that dilatation will progress sufficiently before the appearance of the edema to make the use of Dührssen's incision safe. If the edema is diagnosed sufficiently early so that the patient is not exhausted from protracted ineffectual labor, the prompt employment of this procedure, followed by operative delivery, at this, the most favorable time that can be expected, is advised. If on the other hand the condition is first discovered when the patient is exhausted from long labor, adequate supportive measures and possibly morphine rest should be given before attempts at delivery.

MORTALITY

There was no maternal mortality. Five patients had temperatures of 100.4° F. for twenty-four hours or more. Two babies were stillborn and one died seven hours postpartum, a rate of 14.8 per cent. Of the three infants who died, autopsies were performed on two. In one the cause of death was stated as "intracranial hemorrhage with tentorial tears," the other was reported as "atelectasis neonatorum." In the case of the third baby no autopsy could be obtained, but clinically death was due to cerebral hemorrhage.

SUMMARY AND CONCLUSIONS

Acute edema of the cervix occurring during pregnancy is a very rare obstetric complication, usually of short duration and not a com-

have seen many patients in the past five years who have had pain of long standing with or without urinary symptoms and in whom other tests and examinations were negative, including the intravenous pyelogram but who, after having had the ureter catheterized, had complete and almost instantaneous relief. Stevens¹⁵ claims that this type of case is more likely to be one of urethral stricture. However, if a thorough examination of the urethra has been made prior to the ureteral study, and no stricture has been found, one is scarcely justified in considering the urethra to be at fault.

After eliminating a certain number of patients in whom no diagnosis was made because of incomplete studies and lack of cooperation, a total of 136 patients was available as a basis for this review.

The following tabulation shows the incidence of ureteral stricture occurring among those patients totaling 136, referred to the cystoscopic clinic for study:

	NUMBER	PER CENT
Stricture of ureter	26	19.1
Pelvic inflammatory disease	25	18.3
Sacroiliac disease	24	17.6
Nephroptoses	13	9.5
Gallbladder disease	12	8.8
Hydronephroses	7	5.1
Stone in kidney	6	4.4
Pyelitis	6	4.4
Stone in ureter	4	2.9
Scoliosis	4	2.9
Muscular neuralgia	4	2.9
Retention cyst of ovary	5	3.6
Adenomyoma of uterus	3	2.2

Other conditions occurring only once or twice included: Myoma uteri, postoperative adhesions, syphilis, stricture of urethra, cellulitis of broad ligament, mucous colitis, descensus uteri, endometriomas, incisional hernia and pendulous abdomen. In some cases, more than one diagnosis was present, which accounts for the larger number of diagnoses, than our total of 136 cases. Pelvic inflammatory disease was most frequently encountered next to ureteral stricture. These were usually old cases with doubtful lesions often referred from other departments.

It must be remembered that in this group of patients many were referred from the gynecologic department proper, and other pathology had been largely eliminated; they were usually referred with the provisional diagnosis of ureteral stricture. This possibly accounts for the apparently high number of stricture cases. These cases were selected from a group of clinic and ward patients whose chief symptom was pain in the lower abdomen. We do not include patients in this group who did not have lower abdominal pain, even if they did have ureteral stricture. The group listed under sacroiliac disease also comprises some in whom the diagnoses of lumbar arthritis and scoliosis were made.

It is interesting to note at this time the teaching of the late Dr. J. B. Carnett.²² His views on the subject of abdominal pain are very well

The observations herewith presented refer to patients studied in the Gynecologic Ward and Out-Patient Service of Dr. Brooke M. Anspach at the Jefferson Medical College Hospital. The majority were referred to the cystoscopic clinic in an effort to determine whether or not the cause of the patient's lower abdominal pain was of genitourinary origin. Definite lesions of the pelvic organs (uterus and adnexa) had to be eliminated. The differential diagnosis from so-called "chronic appendicitis" was an equally important factor. A certain number of the patients seen were admitted to the Gynecologic Ward for further study.

The procedure followed in making the examination consisted of: (1) Complete gynecologic history, (2) complete urologic history, (3) abdominal examination, (4) pelvic examination, (5) pyelography, and (6) ureteral catheterization.

In the study of earlier patients, x-rays and pyelograms were not done in every instance, but in the more recent cases attempt has been made to obtain intravenous or retrograde pyelograms whenever possible.

I prefer an intravenous to a retrograde pyelogram in my preliminary study of patients in whom I suspect stricture, because one does not have to contend with the artificial filling and frequent distention of the ureter and pelvis of the kidney incident to a retrograde pyelogram. Furthermore, we do not wish to dilate the ureter with a ureteral catheter prior to viewing a film after excretion urography. In other words, the pelvis, calices and ureters are actually visualized and seen to empty themselves as they normally function.

After the above procedure is carried out, a careful examination is made of the urethra and bladder, and then an attempt made to enter the ureter with a No. 9 or 10 catheter. If this size will not pass satisfactorily, smaller ones are employed until one will pass. If unsuccessful, even with the smallest size catheter, a *provisional* diagnosis of spasm, stricture, valve or kink of the ureter is made, and the patient is instructed to return in a week for further examination. Oftentimes at the second examination even the larger-sized catheter will be found to pass quite readily. If a No. 9 or 10 catheter passes readily without a pull or tug on withdrawal, we do not regard it as a stricture.

Hunner and others rely only on the wax bulb to diagnose stricture, but I feel that if there is a definite obstruction, constriction, stricture, or whatever name may be applied to the condition, it can be diagnosed by one of the larger-sized catheters. Whether or not the x-ray and pyelogram is the final word in the diagnosis of stricture is a debatable question. It would seem to be true that if any type of noncalculous obstruction were present, the ureter would be dilated above the point of constriction. Hunner claims that this is not necessary for diagnosis, and he relies on the characteristic hang on withdrawal of wax bulb. I

I would like to present a few representative case histories to illustrate one or two important points.

CASE 1.—A. M., aged twenty-three years, complained of urinary frequency, pain in vagina and on right side, and dysmenorrhea. These symptoms had been present for several years. She had consulted several physicians and was finally referred to me for ureteral study. Abdominal examination negative, except for deep tenderness over the brim of pelvis on right side. Infected Skene's tubules (repeatedly negative for gonococcus) and congenital erosion of cervix noted. Intravenous pyelogram performed on Mar. 8, 1934, showed a greatly dilated right ureter with constriction at vesical end.

Dilatations of the ureter gave relief to right-sided pain temporarily but soon would recur. Being rather undernourished, and not responding as she should with dilatations, we felt that removal of all foci of infection might aid. We therefore had her admitted to the Jefferson Hospital (August, 1935) and performed dilatation, curettage and cauterization of the cervix, excision of Skene's tubules, and tonsillectomy. The patient was seen again in November, 1935. She was symptom-free and the intravenous pyelogram showed the right ureter to be quite normal. She was still symptom-free in August, 1936. It would appear that in this case, the focal infection had some bearing on the etiology.

CASE 2.—E. H., aged forty years, married. She had one pregnancy in 1922. Soreness in right side since 1923. She was sent to Jefferson Hospital for study. She dated onset of pain since childbirth in 1922 and has had no relief, and during past two years, pain has become worse. Also complained of slight frequency of urination. Pelvis, negative. Intravenous pyelogram showed a hydroureter with a stricture at lower end. On Aug. 14, 1933, a No. 9 catheter was passed and became obstructed 6 cm. above the right ureteral orifice, and her pain was definitely reproduced. August 23, a No. 7 catheter was passed after a No. 9 again failed to pass. August 29, tonsillectomy was performed. The tonsils were small and did not seem particularly diseased. August 31, a No. 8 catheter passed up the right ureter with difficulty after a No. 9 again failed to pass. She had much less pain on right side. Patient was discharged and told to report for readmission in six weeks. Readmitted October 15. She had no more pain. Intravenous pyelogram was repeated and the ureter was found to be normal in size. Patient was discharged. In follow-up visits in April, 1934, and January, 1935, the patient was free of symptoms.

The symptoms in this case date from time of delivery, and I believe that in this case the ureter at the point where it passes through the broad ligament or the tissues in the broad ligament failed to undergo involution properly. In other words, the broad ligament in the region possibly underwent some degree of fibrosis, causing a diminution in the caliber of the lumen of the ureter. It is at this point that most strictures are found in the female, and in our series of stricture cases, in those who had borne children, the obstruction was from 3 to 6 cm. above the ureteral orifice in every instance, while in the nongravid group, the obstruction was higher up in 75 per cent of the cases.

Space does not permit the citation of more case histories, and the cases cited above will serve to illustrate two very important types of cases.

known, but he felt that many cases of abdominal pain were caused by muscular neuralgia, originating in the intercostal nerves. He also believed that most cases of this clinical entity were caused by either (1) lumbar arthritis, (2) scoliosis, (3) exaggerated lordosis or sacroiliac disease, the most frequently offended nerve being the first lumbar.

We are aided in eliminating these factors by the use of the simple tests which he devised, palpation of the tensed abdominal muscles and the pinch test.

Thirteen patients had definite nephroptoses. This diagnosis was not made unless there was a pronounced degree of ptosis and other pathology had been eliminated. Gallbladder disease was encountered 12 times which stresses the importance of complete history and physical examination, prior to special examinations and tests. On analyzing the 26 cases of stricture we found the following: Right side 25, left side 1, married 19, multiparas 14, and nulliparas 12.

In view of the recent studies on the genitourinary tract during pregnancy, we now know that in practically all cases the ureters are greatly dilated and we also know that this is not entirely due to pressure. There is a degree of atony present which can be loosely explained as being hormonal²¹ in origin. Whether or not this is the cause is not pertinent to this discussion, with the exception that possibly the same hormones which cause the uterus to become atonic may also apply to the ureters. After pregnancy is terminated, the uterus, uterine ligaments, and other pelvic tissues involute. We know, however, that no matter how skilled the obstetrician, certain marks of pregnancy remain regardless of how normal the case was or how efficiently the obstetrician repaired the perineum. The question, therefore, comes up as to how much change, which is imperceptible to our senses, has remained after the pregnancy. There are cases in which involution is incomplete and involution now includes also the return to normal of the genitourinary tract.

This might explain some of the cases of ureteral stricture in women who had borne children but not in the nulliparous.

I fully appreciate the pitfalls encountered in establishing a diagnosis of ureteral stricture, and have tried to avoid this by preliminary routine history, physical and pelvic, ureteral study and pyelogram. Oftentimes after these studies, one is in doubt, especially in borderline cases in which the stricture is not sufficiently well developed, to cause a frank distortion on the x-ray plate. It is this type of case that must be watched; if there is no improvement in condition after two or three ureteral dilatations, we make it a point to review the whole case once more and make a more thorough search for focal infection, sacroiliac disease, scoliosis or lordosis, or residual inflammatory disease. Patients who did not respond to treatment, or were doubtful cases, we have not accepted in this series.

tion made on all patients with pelvic lesions, presenting urinary symptoms irrespective of the nature or extent of the pelvic pathology. In the majority of cases, alteration in the urinary tract will be of a purely secondary nature. On the other hand, our efforts will be rewarded in a considerable proportion of cases by finding a lesion in the bladder, ureter, or kidney which may have been unsuspected and which in fact may dominate the entire situation, making the pelvic lesion of purely minor significance.

DR. FAITH FETTERMAN.—In the last four years, since our 1932 presentation, 1,120 cases have been added to our series and the actual incidence of ureteral stricture has been, instead of 44 in 1,164 as in 1932, 23 in 1,120. Our criteria have gradually narrowed and we have decided we must demonstrate an actual obstruction which is not a spasm and not due to irritation.

The interpretation of lower abdominal pain may be helped by three points which we have observed in our clinic. In the first place, all intraperitoneal organs covered or nearly surrounded by peritoneum interpret their pain through the peritoneum, in the form of involuntary abdominal rigidity. Retroperitoneal organs on the other hand manifest their disturbance along the lines of cutaneous nerves or through other viscera. In the differential diagnosis of lower abdominal pain, this point serves to distinguish, for example, pain of appendiceal from that of ureteral origin. Another point is that a ureteral lesion is practically always bilateral in its manifestation. If a careful history is taken, the pain is found to be not one-sided, but generally bilateral. Whether this is sympathetic or actual, I do not know. Another point that has been helpful is that a symptom often observed, namely, pain in the side when the bladder is full, points to a lesion in that ureter. These three points have helped me tremendously in the differential diagnosis of lower abdominal pain even before any urinary tract diagnosis has confirmed urinary pathology.

DR. H. M. GINSBERG.—I believe we lay too much stress on the number of cases seen and forget the fact brought out by Dr. Hunner over fifteen years ago: that obstructed ureters are the commonest cause of obscure abdominal pain in women and that useless operations are continually being performed on these urologic patients.

At the Jefferson Hospital we do not believe that by passing a No. 6 or No. 7 catheter up the ureter you will be able to rule out a strictured ureter unless it is very marked. Furthermore, a large number of patients with this condition are being overlooked, when dependence is placed entirely upon an intravenous pyelogram without a cystoscopic examination. The urinary findings may also be misleading, for very often there are no white blood cells, but specimens collected from the kidney practically always show epithelial cells.

It is very important to study the ureters in persons in whom large doses of radium have been used in the cervix, as very often there may develop a pyonephrosis secondary to a marked strictured ureter.

DR. JOHN McGLINN.—I remember very well the controversies Hunner started when he stressed the necessity of using an air-dilating cystoscope, as against the men who were using water-dilating scopes. At that time I was finding a fair number of strictures because I followed Hunner's method in using air cystoscopes. Keene converted me to the idea that it was a painful procedure to the patient, and after adopting the water type of cystoscope, I found fewer strictures than before.

There is no question that strictures of the ureter occur, even after excluding those which are found after the use of radium for cancer of the cervix. There are a number of patients with lower abdominal pain who are unnecessarily operated

SUMMARY

Twenty-six patients in a series of 136 cases having lower abdominal pain, proved to have ureteral strictures.

Ureteral stricture should be considered as a possible diagnosis in all cases of chronic lower abdominal pain in women.

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DISCUSSION

DR. FLOYD E. KEENE.—When Hunner first reported on ureteral stricture, I was actively engaged in cystoscopic work and despite diligent efforts, I was unable to demonstrate the lesion in anywhere near the high percentage which he reported. During recent years, Eaton has been in charge of this branch of our service and his experience seems to confirm mine. During the last four years, some 1,300 patients have reported to the Cystoscopic Clinic and of these the diagnosis of ureteral stricture was made only 39 times.

Of course, the crux of the matter is one's interpretation of what constitutes a stricture or in other words, upon what data is one warranted in making a diagnosis? I cannot accept the view of Dr. Hunner and his followers regarding the diagnostic importance of what he terms the "hang" on withdrawing the wax tip of a catheter. It seems to me that this may occur in a normal ureter and is but an expression of resentment on the part of the ureter to the trauma incident to the passage of the large catheter. I have always contended that with a stricture of such narrowness as to produce obstructive symptoms, there should be a dilatation of the ureter above the obstruction, particularly if these symptoms be of long standing. To my way of thinking, the evidence which warrants the diagnosis of stricture consists of a tender and often palpable vaginal segment of the ureter, a partial or complete obstruction to the passage of a No. 6 or No. 7 catheter, the reproduction of the typical pain on passing the catheter and the urographic demonstration of a fixed point of narrowing in serial films with dilatation of the ureter above it. In carrying out the diagnosis and treatment of this lesion, one cannot urge too strongly gentleness of manipulation.

I would emphasize one point which this paper brings out and that is the importance of complete urinary studies in cases of obscure pain in the lower abdomen. Many normal ovaries and appendices have been removed through neglect to observe this course, the actual lesion being somewhere in the urinary tract. This applies with equal force to the interpretation of urinary symptoms in the absence of definite pelvic pathology. It has been my custom to have a cystoscopic examina-

of patients receiving treatment with estrogenic factor were not benefited, and it was decided to radiate the pituitary in these cases with the expectation of reducing the pituitary activity, and thus possibly relieving these patients of their symptoms.

In two cases studied by Dr. Spielman he failed to find an appreciable variation in the gonadotropic hormone excreted after the pituitary radiation. However, these tests were carried out at a time when methods of determination were rather crude, so that definite conclusions cannot be drawn. In addition to these two observations, one of us (S. H. G.) had an occasion to study the histology of a pituitary which had been carefully and extensively radiated for a basophilic adenoma. The examination of the gland failed to reveal any histologic changes that could not be accounted for by the sex and age of the patient. However, it is possible that a gland may be physiologically abnormal without this abnormality reflecting itself in a detectable histologic change. Because of the apparent rôle played by the pituitary in the production of the menopausal syndrome, it has been suggested that x-ray therapy, directed toward reducing the activity of the pituitary or in some other way influencing its activity, might be beneficial.

Groedel of Nauheim originally suggested radiation of the ovary in the menopause and reported good results. Subsequently Werner of the Vienna school employed radiation of the pituitary and thyroid either alone or in combination and also obtained good results. Borak and Grabowski also suggested that the combination of pituitary and thyroid radiation might give better results than either alone. Goldhammer and Blass stated that the pituitary radiation does not effect the excretion of gonadotropic hormone in the urine. In addition they had one case in which they could study the morphologic changes in the pituitary gland following radiation but were unable to detect any variation from the normal. Numerous other authors have had similar experiences and results. Collins and his coworkers reported a series of cases, with encouraging results. It must be noted that the follow-up observations in many instances were not of sufficient duration to permit conclusions as to the permanency of the results. In some of the cases a second series of treatments was necessary, and Collins has reported that in this group he obtained permanent success.

We treated a series of 75 patients and in addition utilized an additional 25 cases as controls. The control group was exposed in exactly the same manner as the patients receiving actual treatment except that the rays were screened out. Only one of the 25 control patients reported that she felt better for a few weeks. The other 24 had no beneficial effect. The technic employed at Mount Sinai Hospital was as follows:

	"R" UNITS	K.V.	M.A.	FILTER	FOCAL DIST.	TIME IN MINUTES	SIZE OF FIELD
L. Temporal	150	180	4	$\frac{1}{2}$ Cu. 1 AL.	40	75	6x8
R. Temporal	150	180	4	$\frac{1}{2}$ Cu. 1 AL.	40	75	6x8
Frontal	150	180	4	$\frac{1}{2}$ Cu. 1 AL.	40	75	6x8

upon, and whose condition clears up after the stricture is dilated. Hunner has shown a number of pathologic specimens in which he demonstrated very definitely ureteral stricture. That strictures occur as frequently as he believes, I doubt, because it seems to me that when a catheter is introduced into the ureter, there is apparently a stricture one time and later a perfectly normal ureter.

DR. LINTGEN (closing).—We do not feel that a diagnosis can be made with a No. 6 catheter. I believe that if a No. 9 or No. 10 will pass without reproduction of pain or without a tug when it is withdrawn that there is no stricture present. We do not feel that a wax bulb is essential for diagnosis. Intravenous pyelography does not always tell us the truth because in some cases where the pyelogram was normal, the symptoms cleared up after dilating the ureter. I have not, however, listed any of those cases in my series.

PITUITARY RADIATION FOR THE RELIEF OF MENOPAUSE SYMPTOMS

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DURING the last ten years three thousand cases were observed in the menopause clinic at Mount Sinai Hospital, and we desire to tabulate the response of this large group to various therapeutic measures. We were impressed by the fact that many patients, who regularly menstruated, complained of severe symptoms including flushes, sweats, and other vasomotor and psychic disturbances, as well as those whose menstruation had long ceased.

It has been pointed out by Fluhmann and others that there is an increase in excretion of gonadotropic hormone during the menopause. This may be present with or without unusual vasomotor or psychic disturbances. It has also been shown that an estrogenic hormone may be present in the blood and urine during the menopause, even in those instances where symptoms are pronounced. It is evident that factors other than the withdrawal of estrin or the increase of gonadotropic hormone must be considered as active in the production of symptoms. We do know that following castration, and in the menopause, definite histologic changes, more or less constant, are found in the pituitary. The gland is enlarged and contains the so-called castration cells. It would seem logical that if the pituitary secreted not only an excess of gonadotropic hormone but some other factor, any method that would reduce this excess secretion might be helpful and might control, at least to some extent, the distressing symptoms of the menopause. It has long been suggested by many investigators that the exhibition of estrogenic factor would prove of benefit in the treatment of the menopause syndrome. This has proved to be so, and the result of treatment in a great many cases has been satisfactory. We have noticed that a certain proportion

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEO-ESOPHAGEAL FISTULA (3 CASES)*†

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THE three cases of congenital atresia of the esophagus with tracheo-esophageal fistula herein reported have occurred on the Obstetrical Service of The Long Island College Hospital during the past two years. Either this frequency is unique in our material or the diagnosis heretofore has been overlooked. A knowledge of the characteristic clinical syndrome produced by this malformation should lead to its recognition. Often the symptoms are so typical that a diagnosis can be made soon after the condition is suspected. On the other hand, the aspiration pneumonia which usually results in the death of the infant in from one to ten days frequently is regarded as the primary disease, and in the absence of an autopsy the true nature of the condition accordingly is not discovered.

The author reported the pathologic aspects of eight cases of congenital atresia of the esophagus in 1931¹ and, in collaboration with a pediatrician, presented the clinical aspects of the same cases in 1932.² A survey of the literature shows that clinicians have reported cases soon after attendance at a medical society meeting where the anomaly was presented. This report of three cases is presented not so much to describe a congenital malformation which has been described adequately in the literature many times,³⁻⁶ but rather to call to the attention of obstetricians the frequency of occurrence of the anomaly and the ease with which a diagnosis can be made.

CASE 1.—Baby Girl W. The mother was a twenty-four-year-old primipara who delivered spontaneously and prematurely after a short labor, on May 5, 1934. There was no hydramnios. The placenta showed a velamentous insertion of the umbilical cord. The infant weighed 2,180 gm. at birth and with the exception of a considerable amount of mucus in the pharynx, appeared grossly normal. The nurse noted difficulty in passing a tube for gavage, and feedings were regurgitated through the mouth and nose. On the second day, roentgen visualization of the esophagus after the injection of a barium mixture showed it to end in a blind pouch at the level of the third dorsal vertebra. X-ray examination of the thorax and abdomen on the following day revealed gas in the intestinal tract. A Witzel gastrostomy was performed on the third day. Intermittent distentions of the stomach with repeated respiratory inspirations were observed at the time of operation. This further confirmed the presence of a tracheo-esophageal fistula, first suspected when gas was seen in the intestines on x-ray examination. Clyses and a transfusion were given as supportive measures. Postoperative feedings through the gastrostomy tube caused choking and cyanosis. Respirations became rapid and labored and the infant died five days after birth.

On postmortem examination, the upper portion of the esophagus ended as a blind, hypertrophied pouch measuring 3 cm. in length and 1 cm. in width. There was no cord connecting the upper and lower portions of the esophagus. The lower esophagus measured 3.5 cm. in length and was connected by a fistulous tract to the trachea a few millimeters above its bifurcation into the bronchi. The lungs showed

*Presented at a meeting of the Brooklyn Gynecological Society, November 6, 1936.
†A fourth case has recently occurred in this service.

In the 75 patients treated, there was an equal number of natural and artificial menopause cases. In the artificial menopausal group there was approximately an equal number of surgical and x-ray castrations. We have followed these patients for a period of over two years.

RESULTS

Ninety per cent of the patients lost the hair about the temporal region. In 85 per cent of the cases, sweating, a very common symptom, was markedly decreased and in 20 per cent completely disappeared. Seventy-five per cent of the patients claimed a moderate diminution in the frequency of the flushes. Some stated that after having had 15 to 20 flushes daily they were completely relieved. In 50 per cent of the cases, headaches, either frontal or occipital, were relieved and in some instances apparently cured. In 25 per cent general nervousness and dizziness apparently improved. Palpitation on exertion was relieved in about 10 per cent. The outstanding symptom that was not ameliorated to any degree was the pseudarthritic pain so commonly present. All the above improvements lasted from two to six weeks following a series of three x-ray treatments. The symptoms then gradually returned, though in some instances not as marked as before treatment. It was necessary to continue treatment and in six instances seven series of treatments were given, amounting to twenty-one exposures. Following each series given, an amelioration of symptoms for about six weeks resulted. It was deemed unwise to attempt any additional radiotherapeutic treatment. These patients, when symptoms recurred after the limit of x-ray was given, received injections of progynon-B with marked benefit. This series of patients treated with progynon-B will be reported upon at a later date. Six patients had vaginal bleeding after one application of x-ray to the pituitary. Whether or not this indicates a stimulation of ovarian function through the hypophysis is purely hypothetical. The results obtained by x-ray treatment apparently were in no way dependent upon the duration of menopause.

To summarize, we can say that radiation of the pituitary gland with the technic indicated will invariably relieve the patient for a period of from two to six weeks. The treatment is limited because only a restricted number of exposures can be given. The result of treatment indicates that there is a relationship between the pituitary and menopause syndrome.

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wall was markedly hypertrophied. No cord of tissue was seen extending from this blind end caudally. The trachea, at its bifurcation, was divided into three divisions, two lateral bronchi and a mesial esophagus, which joined the stomach in a normal manner. This portion of the esophagus measured 5 cm. in length and 5 mm. in diameter. Bronchopneumonia was present.

CASE 3.—Baby Boy B. The mother was a twenty-eight-year-old white multipara who had previously delivered two normal infants spontaneously. Hydramnios, first noted in the prenatal clinic, suggested the presence of a monster, but x-ray examination of the abdomen showed what appeared to be a normal fetus. After a normal labor, the patient spontaneously delivered a 2,940 gm. infant on May 16, 1936. The placenta showed no abnormalities.

A large amount of fluid in the mouth and pharynx was noted soon after delivery, and repeated attempts were made to remove it by aspiration. There was constant



Fig. 2.—As described in the text, lipiodol has been forced into the lower portion of the esophagus *B*, through the catheter *A*, and can be seen in the tracheobronchial tree. The tracheo-esophageal fistula is thus demonstrated.

drooling of thick, yellowish brown mucus from the nose and mouth. Many moist râles were heard over the entire chest. On the first attempt to feed the child lactose water, the latter was regurgitated together with a large amount of mucus. Repeated attempts to feed the child were followed by regurgitations. On the second day, an attempt was made to pass a catheter into the stomach, but an obstruction was met. Strong pressure used to force saline through the catheter caused it to return immediately through the nose and mouth. Roentgen and fluoroscopic examination after the introduction of radio-opaque fluid into the esophagus showed a complete obstruction between the second or third dorsal vertebrae. There was a considerable amount of gas in the stomach and intestinal tract, indicating the presence of a tracheo-esophageal fistula. On the third day, a gastrostomy opening was made in the lower half of the stomach, and a tube inserted for feedings. A similar opening was also made in the upper half of the stomach, which was divided

atelectasis and bronchopneumonia. Other than the absence of the innominate vein and the presence of the left anterior cardinal vein, no further abnormalities were noted.

CASE 2.—Baby Boy C. The mother, a thirty-five-year-old primipara, was admitted in labor on Nov. 25, 1935. She was delivered by forceps because of fetal distress. The infant weighed 2,500 gm. at birth and appeared somewhat asphyxiated. The placenta was normal. There was no hydramnios.

On admission to the nursery, a large amount of mucus was noted in the mouth and pharynx. Gavage caused cyanosis and repeated attempts at feeding resulted

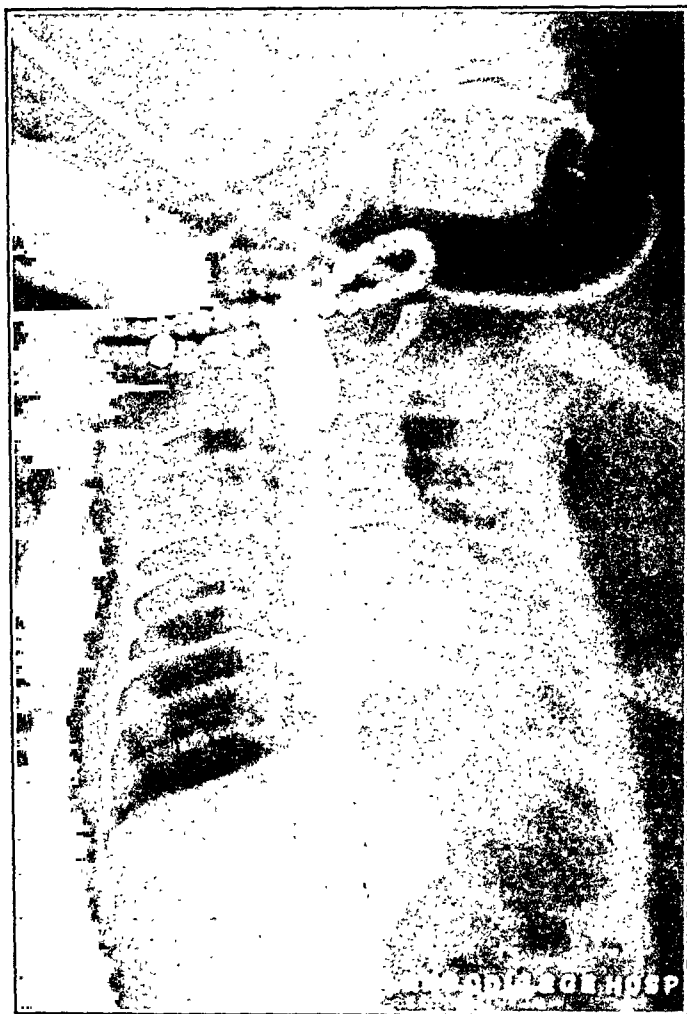


Fig. 1.—The upper esophageal sac has been filled with barium and visualized by the x-ray. Note the presence of gas in the stomach.

in regurgitation through the nose and mouth. On the second day, the infant appeared jaundiced and dehydrated. The diagnosis of atresia of the esophagus was suspected and clyses were given. On the fifth day, roentgen examination of the esophagus, after the injection of a radio-opaque material, showed a definite obstruction opposite the region of the bifurcation of the trachea (Fig. 1). There was a considerable amount of gas in the stomach and small intestines. No operative procedure was attempted. The subsequent course of the child was characterized by progressive cyanosis and dehydration until death occurred on the ninth day.

Postmortem examination showed the upper portion of the esophagus to be represented by a blind pouch measuring 4 cm. in length and 1 cm. in diameter. Its

After the death of the child, a catheter was tied in the lower portion of the esophagus and 10 c.c. of lipiodol was injected into the lower portion of the esophagus while pressure was made on the larynx. The striking x-ray demonstration of the tracheo-esophageal fistula may be seen in Fig. 2.

Postmortem examination revealed the upper portion of the esophagus to end in a blind pouch measuring 3 cm. in length and 1 cm. in diameter. The wall was moderately hypertrophied. The trachea was divided into three tubes, two lateral bronchi and a mesial tube, which formed the lower portion of the esophagus. This part of the esophagus measured 6 cm. in length, 5 mm. in diameter, and joined the stomach in a normal manner. The stomach was divided as noted above and each portion showed a stoma. The respiratory tract showed tracheobronchitis and bronchopneumonia. An anomaly of the right thumb was also noted.

A detailed account of the gross and microscopic pathology, a recapitulation and discussion of the theories of development of the anomaly, and a presentation of a new interpretation, based on studies of human embryos from the collection at the Carnegie Institution of Washington, have been previously reported.¹ Within an experience of six years, eleven gross specimens of the anomaly have been examined by the author. All have closely resembled each other, showing the morbid anatomy of this malformation to be markedly constant.

SUMMARY AND CONCLUSIONS

1. Three cases of congenital atresia of the esophagus with tracheo-esophageal fistula have occurred within a period of two years on an obstetric service where 1,200 women are delivered yearly. It is probable that many cases escape true diagnosis.

2. The obstetrician often has the opportunity of observing the first clinical sign of the malformation, namely, the presence of a large amount of mucus in the mouth and pharynx of the newborn, and difficulty in clearing the respiratory passages by aspiration.

3. The most characteristic and constant symptom is the regurgitation that occurs after each feeding, often accompanied by coughing and cyanosis.

4. The diagnosis can be easily confirmed by the passage of a catheter into the esophagus and roentgen visualization after the introduction of a radio-opaque fluid.

I am deeply indebted to Dr. George W. Phelan and to Dr. Morris Glass for their kind permission to report their cases.

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from the lower by a row of sutures running from the lesser to the greater curvature. During the operation, while the stomach was open, repeated inspirations of the infant were noted to cause bubbling from the gastrostomy wound, confirming the presence of a tracheo-esophageal fistula. The operative procedure was conceived and performed by Dr. Albert Ritzmann, resident surgeon at The Long Island College Hospital, who will report this case from a surgical viewpoint.

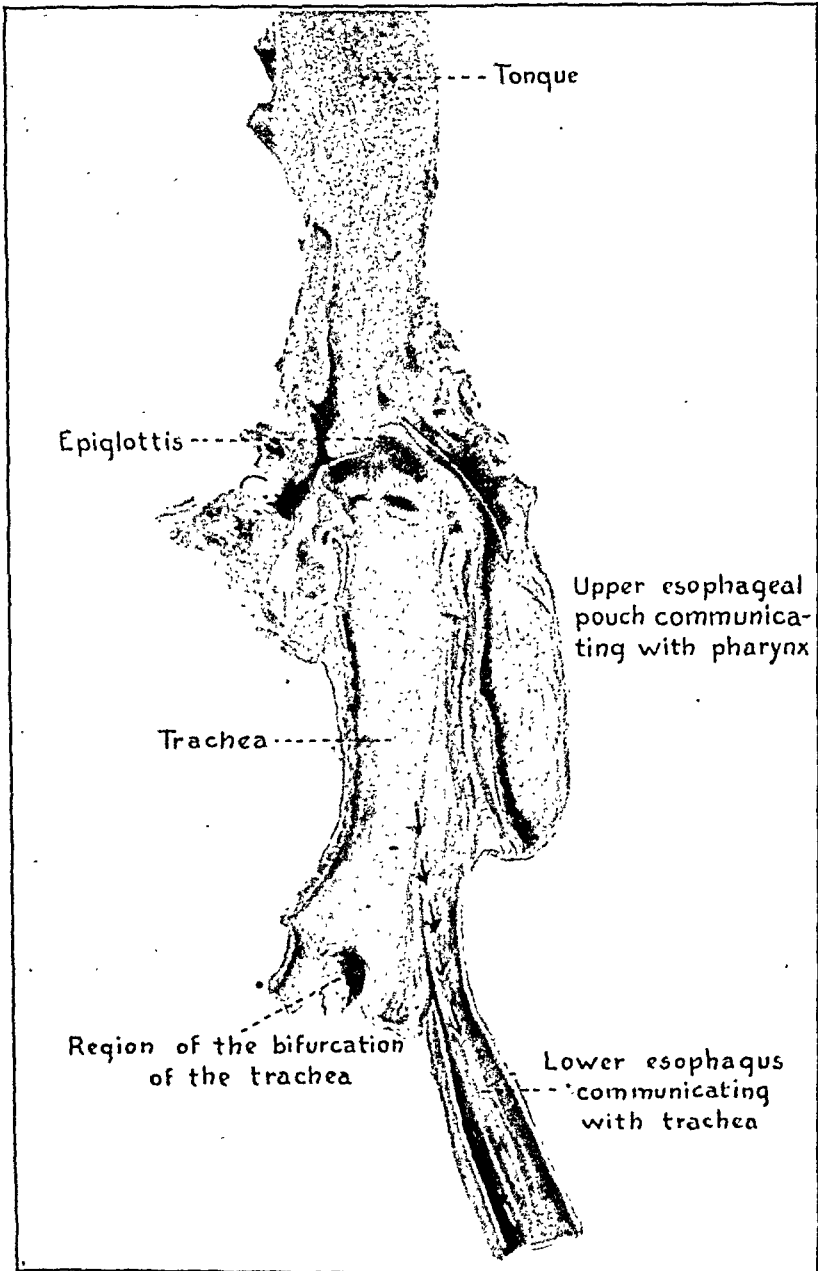


FIG. 3.—A retouched photograph of a specimen reported previously, showing the characteristic gross morphology of the malformation.

Postoperatively, the child did well. Mucus still came from the nose and mouth but the chest was relatively clearer. Feedings were taken well through the gastrostomy tube and did not cause the choking and cyanosis noted in the case of Baby W. Four days after operation, however, the general condition of the child became poorer. The chest was again filled with moist râles and attacks of cyanosis were noted. The child died on the eighth day of life.

Physical Examination.—The patient was a well-developed and fairly well-nourished young white adult female. The heart, lungs, head, extremities, neck, and skin were normal. The breasts were well developed. The areolae were dark pink and no secretion could be expressed from the nipples. The reflexes were normal. There was no enlargement of the superficial lymph nodes. By abdominal examination a cystic, regular, nontender mass was palpable in the right lower quadrant of the abdomen. No other masses or organs were palpable. Inspection showed an introitus of marital type and a mucosa of normal color. The cervix was soft and not lacerated. By bimanual examination the uterus was normal in shape and consistency but slightly enlarged. The left adnexa was normal. In the posterior culdesac there was a large, semisoft, slightly tender mass, apparently connected with the right tube and ovary and almost completely obstructing the rectum. The uterus was anterior and to the left of the mass. There was no blood.

Laboratory Findings.—A catheterized specimen of urine was normal. Wassermann and Kahn tests were negative. Blood examination showed 3,250,000 red cells with 68 per cent hemoglobin and 5,200 white cells with 80 per cent polymorphonuclear leucocytes, 17 per cent lymphocytes, 2 per cent large mononuclear leucocytes, and 1 per cent eosinophiles. A Friedman test was positive (Feb. 26, 1935).

Operation.—After a preliminary transfusion of 450 c.c. of citrated whole blood, on Feb. 27, 1935, the abdominal cavity was opened through a low midline incision. A hemorrhagic cyst about 16 cm. in diameter was found adherent by a soft vascular friable base to the uterus and tissues of the posterior culdesac. The tumor was removed with difficulty and much difficulty was encountered in controlling the generalized ooze of blood over the area from which the mass was stripped. This was eventually well controlled. The right tube was removed with the tumor mass and appeared normal. The right ovary was not identified. The left tube and ovary were normal. The uterus was normal in size and shape.

Pathologic Report.—*Gross:* The specimen consisted of a rounded partly encapsulated mass of old blood and soft gray tissue apparently situated in the broad ligament. The attached tube was slightly congested and edematous. On section the lumen of the tube appeared normal and the fimbriated end was free. There was no gross evidence of ovarian tissue.

Microscopic: Sections of the soft gray portions of the cystic mass showed a typical chorioma consisting of irregular Langhan's cells and syncytium. A section of the tube showed no evidence of tumor. The blood vessels were congested and there was slight edema of the tube wall. The mucosal folds were delicate and essentially normal. No ovarian tissue was found.

Diagnosis.—Chorioma of ovary. Congestion and edema of tube.

Postoperative Course.—The patient recovered from the operation for about ten days; then she began to fail rapidly, the red blood cells and hemoglobin going down steadily in spite of three more blood transfusions. About her fifteenth postoperative day she developed pain in the chest, followed by hemoptysis. X-ray showed metastases to the lungs. Another Friedman test at this time was strongly positive. The patient died twenty-one days after operation.

Postmortem Examination.—March 22, 1935. One and one-half hours after death.

The body was that of a fairly well-developed and emaciated adult white female 166 cm. long. No rigor mortis was present and there was very slight lividity. The pupils were round, regular, and unequal. The left measured 0.5 cm. and the right 0.3 cm. in diameter. The nose, ears, and mouth were not remarkable. No superficial lymph nodes were palpable. A midline lower abdominal scar extended 14 cm. above the symphysis and a small sinus 1 cm. in diameter was present, near its lower end.

PRIMARY CHORIOMA OF THE OVARY

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THAT primary chorioma may develop in extrauterine sites following pregnancy is adequately proved by numerous isolated records, although the incidence is very low. About 2.6 per cent of choriomas are preceded by ectopic pregnancy.¹ The histogenesis of others is explained on the basis of hematogenous transportation of normal placental elements from the uterus to different parts of the body where they subsequently undergo malignant change.² A still smaller group of primary ectopic choriomas arise without any preceding pregnancy and are of teratomatous nature, their origin in the ovary being analogous to chorioma of the testis. Klaften³ collected reports of 7 such ovarian tumors occurring in females whose ages varied from seven to eighteen years, and adds a complete record of an ovarian chorioma in a child of eleven years who came under his observation. In all 8 of these cases the factor of pregnancy was adequately ruled out. Most of the tumors in this group as well as in a somewhat larger group of adults consist not only of chorioma but also of an admixture of other tumor elements derived from one or more germ layers. In addition to the cases reviewed by Klaften, Maki and Takeda⁴ report a case of primary ovarian chorioma in a twenty-one-year-old virgin.

The following case is placed on record because of the rarity of primary ovarian chorioma and as a basis for discussing several diagnostic problems:

M. D., a married white female, aged twenty-two years, was admitted to the St. Francis Hospital on Feb. 18, 1935, with the complaint of lower abdominal pain and vomiting. The family history was irrelevant. There was a remote history of measles and tonsillectomy. She had leucorrhea during the past year and a Bartholinian abscess was incised and drained in March, 1934. Menses were established at the age of fourteen and had been regular, painless, and of four days' duration every twenty-six to thirty days until February, 1934, when there was amenorrhea for six weeks followed by sudden onset of bleeding with the passage of clots, lasting fourteen days. Menses were then resumed at regular intervals until the present illness. Her last normal period occurred on Nov. 18, 1934, and lasted four days. A normal amount of blood was passed without clots and without pain. She had been married for two years but never, to her knowledge, had been pregnant.

Present Illness.—On Dec. 1, 1934, vaginal bleeding occurred two weeks prior to the expected period and continued throughout the month with the passage of a moderate amount of blood. There was no bleeding during January. On Jan. 14, 1935, there was a sudden onset of right lower abdominal pain radiating to the back. She became weak and fainted but passed no blood. Following this she had discomfort in the lower abdomen. Morning nausea and vomiting and slight tenderness of the breasts without appreciable enlargement were noted two weeks later. Vaginal bleeding again occurred on Feb. 6, 1935. It was painless, there were no clots, lasted one week and was interpreted by the patient as menstruation. No blood was passed by vagina after this. Slight dysuria and severe constipation developed rapidly and she came to the hospital on Feb. 18, 1935.

Urinary Organs: The kidneys were similar and about twice normal size, due to numerous tumor nodules distributed throughout each kidney (Fig. 2). The calices, pelves, ureters, and bladder were normal.

Genital Organs: The external genitals were not remarkable. The labia minora and vagina showed no evidence of pathology. The cervix was normal in size and shape and the lips around the slitlike os were slightly soft in consistence. The fundus of the uterus was normal in size and symmetrical. The wall was of normal thickness. The endometrium was grossly normal and showed no evidence of tumor. The left tube was normal in appearance. The left ovary showed no evidence of corpus luteum and appeared as a fibrous and cystic mass 2 cm. in diameter. The right tube and ovary were absent and in their place was a soft friable dark red mass of tissue similar to the tumor described elsewhere. This tissue was mixed with old blood clot and apparently extended forward to the sinus in the anterior abdominal wall.



Fig. 2.—Metastatic chorioma of kidney.

Aorta: Smooth and elastic throughout.

Bones: The ribs appeared normal. Superficial inspection of the spine from the anterior surface and the inner wall of the pelvis showed no evidence of bone metastases.

Lymph Nodes: The abdominal lymph nodes were slightly enlarged, but showed no evidence of tumor.

Summary of Anatomic Diagnosis.—Metastatic chorioma from ovary to lungs, liver, kidneys, and intestinal tract. Anemia.

Histologic Examination.—

Heart: Normal.

Lung: Invaded by numerous masses of tumor cells. The tumor consisted of two types of cells, one resembling Langhans' cells and the other resembling syncytium.

Peritoneal Cavity: The surfaces were smooth and glistening and slightly discolored with old blood, except in the pelvis where, on the right side, there was a soft mass of dark red friable material which extended from the region of the right ovary to the sinus in the anterior abdominal wall. The viscera were normally disposed. The mesenteric lymph nodes were not enlarged. The diaphragm extended to the level of the fifth rib on each side. The liver projected 2 cm. below the left costal margin, 9 cm. below the xiphoid and 5.5 cm. below the right costal margin.

Pleural Cavities: The left pleural surfaces were smooth and glistening. There were no adhesions or free fluid. The right pleural surfaces were dull and injected. About 25 c.c. of turbid yellow fluid were present. There were no adhesions.

Pericardial Cavity: The surfaces were smooth and glistening. There was a slight excess of thin yellow fluid present. There were no adhesions.

Heart: Normal in shape and position. Slightly dilated. The epicardium was thin and transparent. The myocardium was homogeneous, pale red in color, of normal thickness and soft in consistence. The endocardium was thin and transparent. The ventricles were slightly dilated. The valves and coronary arteries were normal.

Lungs: Both lungs contained numerous round soft dark red tumor nodules distributed throughout. Most of these ranged between 1 and 2 cm. in diameter (Fig. 1).



Fig. 1.—Metastatic chorioma of lung.

In the right upper and middle lobes there was a similar nodule about 6 cm. in diameter which extended between the two lobes. The pleural surfaces over this nodule were dull, injected, and covered with fibrin. The lung tissue surrounding the tumor nodules was essentially normal.

Spleen: About twice normal size. The capsule was thin over a smooth dark purple surface, except at the lower margin where there were a few rough projections of tumor similar to that described elsewhere. These tumor masses were about 0.5 cm. in diameter and no others were found in the spleen substance.

Pancreas: Normal in size, shape, color, and consistence.

Liver: Normal in size, shape, color, and consistence. On section three round, dark red, soft nodules of tumor were found in the liver substance. The gallbladder was thin walled and grossly normal.

Gastrointestinal Tract: Two small tumor nodules were present in the wall of the ileum and an elongated mass of tumor material appeared as a thrombus in a small vessel leading to the larger of these masses. On the mucosal surface the larger mass was ulcerated and covered with blood clot. The small intestine contained masses of blood clot and the contents of the larger intestine were black in color.

Adrenals: Normal in size, shape, color, and consistence.

against it. The positive Friedman test was strong support of the diagnosis of ectopic pregnancy and the operation was planned on the basis of this diagnosis. Another problem in diagnosis presented itself at operation when it seemed apparent that the tubes were essentially normal. The absence of fetus and membranes in so large a mass led to the diagnosis of tumor. This was confirmed by microscopic examination of the surgical specimen. Aschheim⁵ demonstrated that the content of anterior pituitary hormone in the urine is far higher in chorioma than in normal pregnancy. While a routine Friedman test is of no value in differentiating chorioma from hydatidiform mole or pregnancy, a persistently positive test after removal of all gross tumor is valuable evidence that removal was actually incomplete. The rapidly fatal outcome following the second positive test was, therefore, expected.

The case reported here brings up the academic question as to whether the tumor arose from the placental remnants of a pregnancy two years previous or as a teratoid tumor from the ovary. In assuming the former, one must consider the possibility that the remains of a pregnancy within the uterus disappeared. An undestroyed placental fragment transported to the region of the ovary may then have become malignant. Another possibility is that an ectopic pregnancy either in the tube or ovary may have terminated in a similar manner, the passage of clots being the result of the loosening of endometrial decidua. It seems unlikely that a tubal pregnancy could have ruptured or aborted and leave the tubes with no evidence of damage. Although an interval of two years between pregnancy and the appearance of tumor is unusual, a latent period of several years does not argue against the relationship between the two. The disappearance of primary uterine chorioma has been authentically reported⁶ and may be applicable to the case reported here. The question as to whether the tumor was related to ovarian pregnancy or originated as a teratoma cannot be answered. The surgical specimen was subsequently reviewed in an effort to find teratomatous tissue other than chorioma, but without success. However, in the reported cases the chorionic elements of a teratoma had frequently so outgrown the other tissue that the latter were hard to find. It appears, therefore, that the case is one of primary chorioma of the ovary.

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2222 WEST SEVENTEENTH STREET

Antoine, Tassilo: *Pseudomyxoma of the Peritoneum*, *Ztschr. f. Geburtsh. u. Gynäk.* 111: 37, 1935.

The author presenting seven additional cases seen since 1931 states that pseudomyxoma of the peritoneum may arise from either the appendix or the ovary, and that the condition has been found in both organs simultaneously. The gelatin-like secretion comes from the epithelium and penetrates the connective tissue by a rarefaction of the latter and a compensatory filling of the spaces with the material. The prognosis is bad in advanced cases, the patients dying slowly of cachexia. The treatment consists of radical surgery followed as soon as possible by several courses of deep x-ray therapy of cancer intensity.

EUGENE S. AUEL.

There was marked variation in the size and shape of the tumor cells and each mass was associated with hemorrhage. A few small branches of the pulmonary vessels were occluded with minute tumor thrombi.

Spleen: A section including the roughened peripheral portion showed a mass of irregular cystic spaces filled with flat cells resembling endothelium. The cysts were filled with serous fluid. There was no evidence of metastatic tumor. These cysts apparently represented lymphangioma. Elsewhere the spleen appeared normal.

Pancreas: Normal.

Liver: A section including one of the metastatic tumor nodules showed typical chorioma (Fig. 3).

Adrenal: Normal.

Kidney: The tumor nodule in the section studied was associated with an extensive hemorrhage. Elsewhere the convoluted tubules and capsular spaces were markedly dilated.



Fig. 3.—Photomicrograph of metastasis in liver.

Left Ovary: Most of the organ was fibrotic. There were a few remnants of corpus luteum, one of which was cystic. The follicles were all very poorly developed.

Uterus: The muscle cells appeared to be of normal size and arrangement. The blood vessels were not remarkable. The endometrium was normal in thickness and the glands showed a normal arrangement. The interstitial cells were likewise normal and showed no evidence of decidua reaction.

Small Intestine: In the section studied there was a metastatic tumor nodule invading the wall and ulcerating the mucosal surface.

Head: Permission to examine the cranial cavity was not granted.

DISCUSSION

On admission, provisional diagnosis of ruptured ectopic pregnancy or ovarian cyst with twisted pedicle was made on the basis of the history of sudden severe abdominal pain and the finding of a mass in the left lower quadrant. The differential diagnosis was confused by the history of morning nausea and vomiting and tender breasts which suggested pregnancy and the presence of menstruation which was

nonreducible. No cough impulse. Appeared to be connected to a large spheroidal mass which occupied the entire lower half of the abdomen. This mass was the size of a five months' pregnancy.

Vaginal examination showed a pelvic mass reaching to the umbilicus, extending three fingerbreadths to the right side and four fingers to the left, hard and tender. Adnexa not felt. The pelvic floor was relaxed. The cervix was underneath the

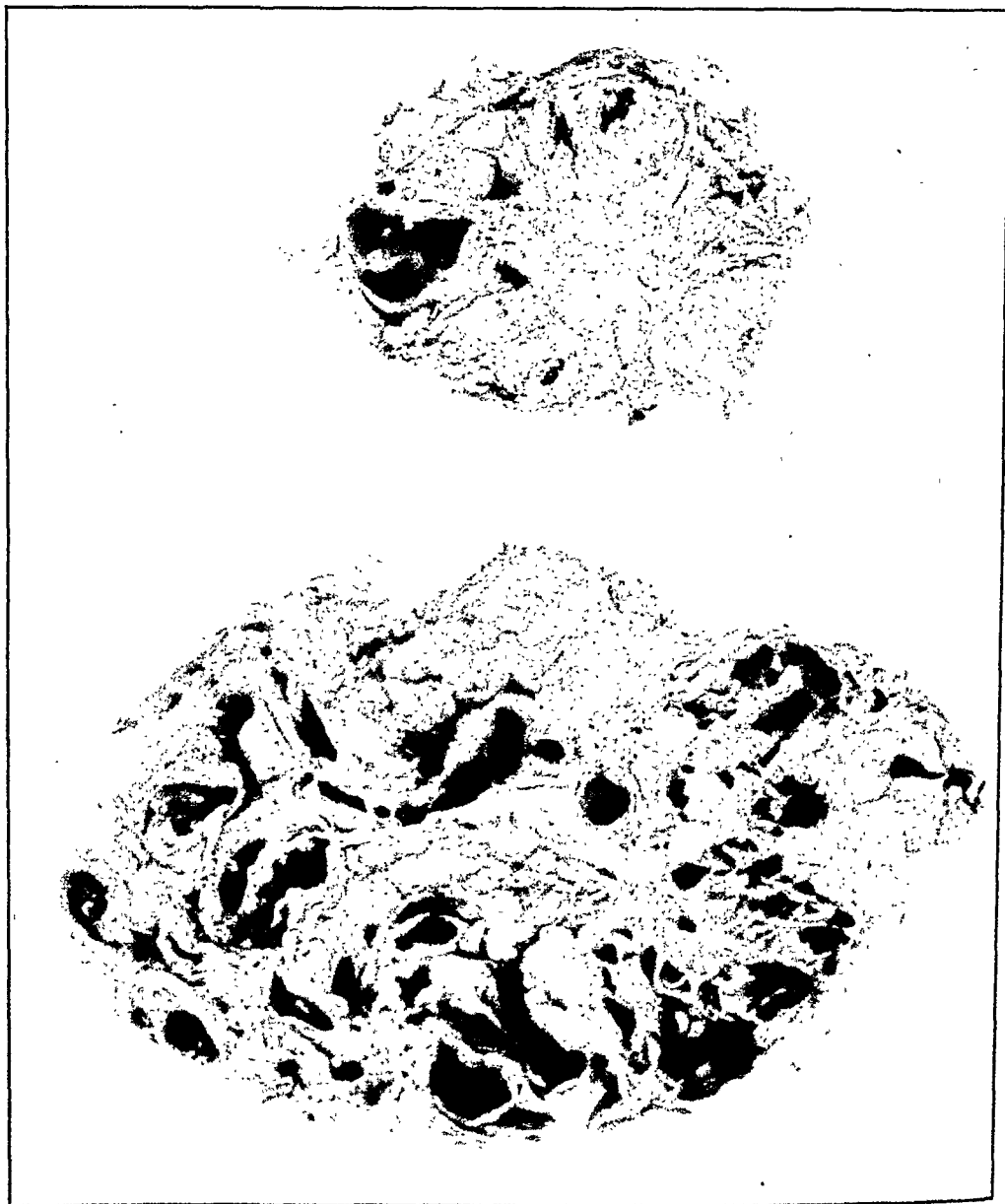


Fig. 1.—Gross specimen of bilateral ovarian tumors.

symphysis and bilaterally lacerated. There was a serous discharge present. Uterus was incorporated in mass described above. A soft mass, the size of a grapefruit, was present in the culdesac, which felt cystic.

A diagnosis of fibromyoma uteri and ovarian cystoma was made.

Operation by Dr. Ogintz.—Excision of old scar and abdomen entered. A small, dark red, friable mass was encountered in the incision. This mass was similar in character to the intraabdominal masses. The uterus was moderately enlarged, and

GRANULOSA CELL TUMOR WITHOUT UTERINE BLEEDING

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WITHIN recent years, granulosa cell tumors have received much attention by gynecologic pathologists. These tumors are, undoubtedly, not as rare as was once thought. Since more has been learned about their physiologic effects, their recognition preoperatively has become more simple; and since their morphologic characteristics are being more carefully studied, the pathologic diagnosis is made more often than formerly.

Since Robert Meyer⁸ first emphasized the physiologic effects of these tumors, another cause of menstrual irregularity and postmenopausal bleeding has been discovered. A recent analysis of thirty-six cases by Novak and others, has pointed out characteristic menstrual disturbances which seem to fall in age groups. One interesting point which has a direct bearing on this case report is that cases occurring after the menopause produce periodic or a pseudomenstrual type of bleeding. Details of this have been brought out by another recent study of postmenstrual bleeding in granulosa cell tumors by Novak and Brawner.¹⁰ These disturbances of the cycle are due to the production of theelin by granulosa cells which arise from the ovarian mesenchyme, whether they are of epithelial or connective tissue origin. Biologic hormone studies of the blood and the urine have disclosed that these tumors are capable of secreting the hormone of the granulosa cell. A detailed discourse of the history, pathology and pathologic physiology is not necessary as it has been adequately covered in other papers.

An interesting feature of these tumors is that the majority reported thus far have been unilateral. In Novak's series, which is a rather large series of cases, only two were bilateral in character and only one of these cases presented a second tumor of any appreciable size. Eighty cases studied by Klasten⁴ indicated that only five cases were bilateral. One-hundred and one cases studied by Szathmary⁵ indicated that only 10 per cent were bilateral.

The reasons for reporting the following case are:

1. Well-developed bilateral ovarian granulosa cell tumors were found.
2. These tumors occurred in a woman three years past her menopause, during which time she had no vaginal bleeding.

A fifty-year-old colored female was admitted to the Gynecological Service at Kings County Hospital on Feb. 11, 1936, complaining of a small lump in an old lower abdominal incisional scar since July, 1935. She claimed it varied in size and at times it became tender. She complained of nausea, vomiting, chills, and fever.

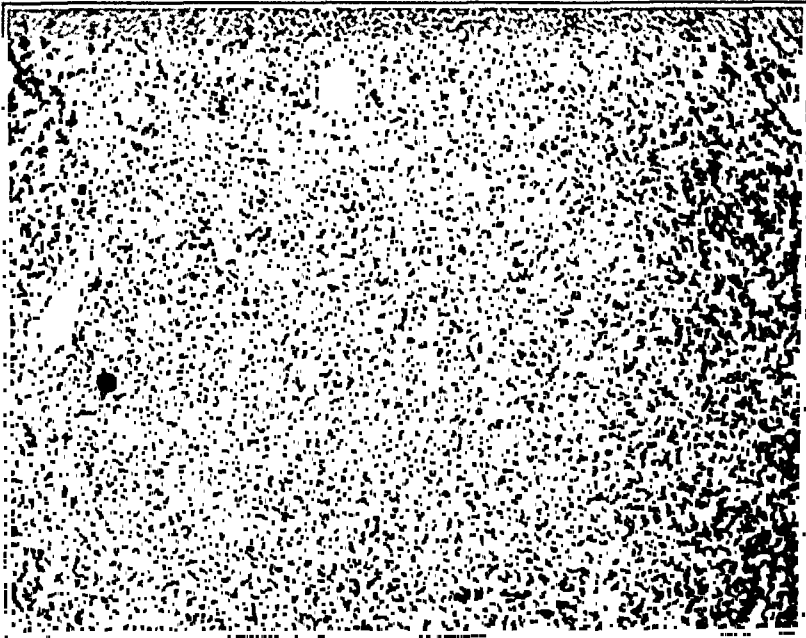
There has been an associated loss of weight (patient could not tell how much) and a dragging pain in the back. There was no vaginal bleeding or discharge. The cardiorespiratory systems were negative.

The patient had never been seriously ill. She was operated upon (on uterus) fourteen years previously. Does not recall type of operation done. Menses 14 x 28 x 3-4 regular. No dysmenorrhea. Venereal disease denied. She had had 8 pregnancies. Menopause, last bleeding three years ago; menopause accompanied by diminishing periods and vasomotor symptoms.

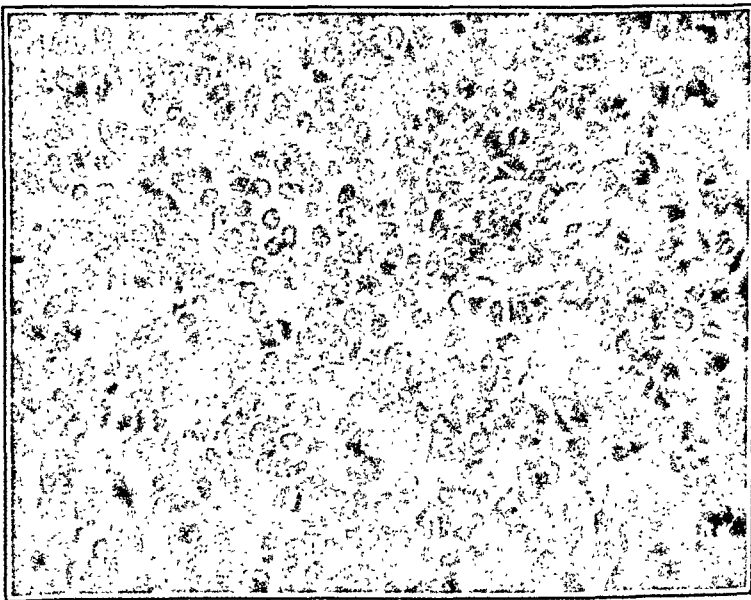
The abdomen was obese. Liver and spleen not felt. In the middle of a lower midline incision a hard mass, measuring 2 x 1½ inches, was present, tender and

which were lined by apparently granulosa cells. No histologic evidence of corpus luteum was found. The entire tumor was surrounded by a definite fibrous capsule.

Histologic examination of the hemorrhagic fragments showed a diffuse growth of granulosa cells which were closely packed together and did not appear to form any follicular or rosette areas. These fragments were extremely vascular, and there were large areas of hemorrhage throughout.



A.



B.

FIG. 3.—A, Rosette type, lower power. B, Rosette type, high power.

Diagnosis: (A) Granulosa cell carcinoma of ovary and (B) metastatic granulosa cell carcinoma.

Present Status.—The patient was seen Sept. 26, 1936. Since the operation she stated she felt well and has gained fifteen pounds. Her appetite was good. Her only complaint was occasional urinary frequency and nocturia.

no fibromyomas were seen. A large mass in the region of the right ovary; a second smaller mass adherent to the sigmoid; a third mass below this, was deeply embedded in the sigmoid. Tubes appeared to be normal.

The first two masses were freed and removed by clamp and suture. The third could not be mobilized for removal. Operative diagnosis: Bilateral carcinoma of the ovaries.

The postoperative course was uneventful. Beginning March 3, 1936 she was given 10 treatments of 200 r. units at a 40 cm. distance. Further treatment was refused by patient. She was discharged March 26, 1936 in an improved condition.

Surgical Pathology.—Gross Specimen: Specimen consisted of two tumors, one measuring 5 by 5 cm.; the other 3 by 2 cm. (Fig. 1). They were ovoid in shape and well encapsulated in a fibrous capsule. Both tumors on cross-section were similar in character. They consisted of islands of grayish, opaque, firm tissue with large irregular hemorrhagic areas. These various areas were encapsulated by strands of light brown and gray fibrous tissue. Isolated areas of light brownish



Fig. 2.—Diffuse type. High power.

tissue were also noted. Several small cysts filled with clear fluid were also seen in both tumors. Several small pieces of reddish gray tissue, having the same general appearance, Fig. 1, were noted, and taken from the abdominal scar.

Gross Diagnosis: Granulosa cell tumor of both ovaries with metastasis to abdominal scar.

Microscopic Pathology.—Examination of the tumors showed a markedly varying histologic picture. In both tumors evidence of ovarian tissue was noted, in which old corpora albicantia were still present. The newgrowth, for the most part, was of a diffuse type made up of polyhedral cells and irregular columns of cylindrical cells with ovoid and round nuclei, containing a fairly large amount of chromatin, distributed irregularly throughout (Fig. 2). Here and there mitotic figures were seen. The cytoplasm was light pink-staining and granular in character. Definite primordial follicular configurations were noted, with a radial distribution about the lumen (Fig. 3). Other areas showed a mixture of cells growing in a cylindromatous character and, also, small groups of rosette configuration (Fig. 4). The tumor throughout was extremely vascular, and numerous large blood channels were noted

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PERIPHERAL GANGRENE FOLLOWING PREGNANCY

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THE occurrence of gangrene of an extremity following pregnancy is so unusual that a review of the literature up to and including 1934 revealed only 102 cases. The largest individual contribution was that of O. Schmidt¹ (1921) who reported 3 cases. Since we have had 3 such cases within a period of five years, I believe they are worthy of being recorded.

CASE 1.—J. D., aged thirty-seven, gravida vii, para v. Previous pregnancies terminated in normal deliveries with the exception of two spontaneous uncomplicated abortions at three and two and one-half months, respectively. Last pregnancy three years previous to present admission.

Patient attended the antenatal clinic where her course was uneventful. During the last month of pregnancy she developed painless swelling of the left lower extremity.

On admission, irregular uterine contractions were present. The uterus was enlarged to the size of a full-term pregnancy, and an average-sized fetus was found presenting in the L.O.A. position. Temperature and pulse were normal. Blood pressure 116/78 and urinalysis negative.

The only other physical finding of note was marked swelling of the left lower extremity with tenderness along the course of the saphenous vein and beneath the left Poupart's ligament, thought to be due to venous thrombosis.

She delivered spontaneously a normal full-term fetus after a six-hour labor. For the first seven days postpartum her course was satisfactory. The tenderness and swelling in the left leg improved gradually and the pulse and temperature remained within normal limits. On the second day postpartum, one gynergin tablet (ergotamine tartrate gr. 0.008) was given every four hours, the indication being profuse lochia. This medication was continued until the morning of the eighth day postpartum, a total of 32 doses in all.

On the eighth day she began to complain of pain in the left foot and it was found that the latter was cold, cyanotic and slightly tender. At this time her pulse rose to 120 and temperature to 100° F.

A diagnosis of arterial thrombosis with impending gangrene was made and conservative treatment was instituted. Temperature remained in the neighborhood of 102° with gradual return to normal in ten days. Dry gangrene involving the entire left foot was present with the line of demarcation appearing just above the ankle. Three weeks after onset of gangrene a midleg amputation was performed with an uneventful recovery.

Examination at that time showed a well-nourished patient. Abdominal examination showed no masses. Gynecologic examination disclosed a relaxed perineum. There was evidence of a cystocele. The cervix presented a chronic endocervicitis. The uterus was moderately enlarged. No masses were palpable. Rectal examination was negative. A Friedman test, done at that time, was negative.

DISCUSSION

The reason why this woman did not have menstrual bleeding cannot be definitely explained. No evidence of a corpus luteum variant of the tumor was found either grossly or microscopically, so that production of progesterin as a cause for the continued amenorrhea can be discounted. Histologically, the tumor was made up of epithelial granulosa cells, assuming three types of growth: (1) diffuse; (2) immature follicles and (3) cylindrical. Although no biologic assays were done for folliculin, judging histologically from the type of cell, the folliculin levels must have been high.

The more recent explanation of menstrual bleeding of a folliculin level sufficient to inhibit the anterior pituitary, thereby producing depressing ovarian activity, is also

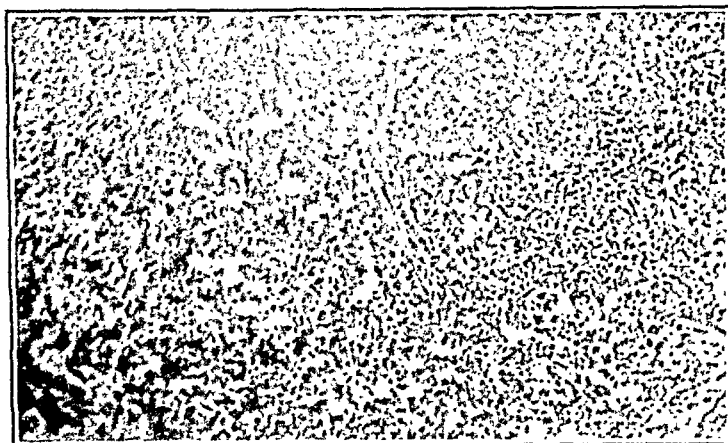


Fig. 4.—Cylindrical type, low power.

insufficient to explain the amenorrhea, because the extent of the tumor involvement and histologic character, as stated above, must have produced levels of folliculin capable of pituitary inhibition. The enlarged uterus in the gross absence of fibromyomas is indirect evidence that folliculin was produced and was active on the uterus. Unfortunately, a curettage was not done, which might have yielded further evidence of follicular activity upon the uterus.

Two cases of granulosa cell tumor with amenorrhea have been reported in the literature. One case, studied by Benda and Krans,² was of a patient thirty-eight years of age with an amenorrhea of two years' duration. They were under the impression that this tumor was producing the lutein hormone because, histologically, the tumor was made up predominantly of lipoid-laden cells with characteristics of lutein cells. The menses returned after operation. The other case was studied by Szathmari.³ This occurred in a woman sixty-three years of age, in which they found a tremendously hypertrophied uterus. They felt that the reason for her amenorrhea was because of a greatly hypertrophied endometrium with marked necrosis, producing a disturbed circulation.

and pulse remained normal. In view of marked improvement, she was allowed out of bed on the afternoon of the twelfth day postpartum, four days following the onset of pain in the lower extremity.

Shortly after leaving bed the patient was again seized with a severe pain in the left leg, again requiring morphine for relief. Pain continued for thirty-six hours following which it was noted that the entire left extremity was discolored from the knee to the toes; the same area was cold and cyanotic. The dorsalis pedis and popliteal arteries were not palpable. Thrombosis of the femoral artery was diagnosed, and an immediate arteriotomy was decided upon.

At operation the left femoral artery was exposed in the region of Hunter's canal. The vessel walls were found thickened and rigid with no pulsations present. The artery was incised and a thrombus removed, following which blood spurted from the proximal end of the vessel. The popliteal artery was then exposed through an incision in the popliteal region. On incision this vessel was found to contain a well-organized thrombus which was removed by injecting saline through the upper incision and allowing it to flow through the popliteal incision. The arteries were closed with paraffinized black silk.

The following day her condition showed no improvement; cyanosis and coldness persisting in the extremity. During the following five days the line of demarcation of dry gangrene gradually appeared at the junction of the mid and lower thirds of the leg. A midleg amputation was performed six days following the arteriotomy. Patient remained well for three weeks following the amputation when she began to complain of pain and numbness in the right foot. Examination revealed slight swelling but no cyanosis. The right popliteal and dorsalis pedis arteries were not palpable. Impression was thrombosis of the right popliteal artery. Elevation of the leg together with dry heat and diathermy treatments was immediately instituted and continued for four days. The pain gradually subsided and she was discharged from the hospital two weeks later in good condition.

Pathologic examination of the amputated extremity revealed an extensive phlebo- and arteriosclerosis.

Previous to the onset of gangrene in this patient we could find no evidence of infection to account for its occurrence. In casting about for some other possible explanation for the thrombosis we were led to wonder what rôle, if any, the occurrence of eclampsia might have had. In reviewing the previous reports, it was found that puerperal gangrene had been preceded by eclampsia in 6 of the cases.

Blackman⁴ reports a case of severe eclampsia during labor in an eighteen-year-old primipara followed by gangrene of both extremities on the third day postpartum. At autopsy the abdominal aorta was found thrombosed 2 inches above its bifurcation.

Lugeol's⁵ case was one of severe intrapartum eclampsia followed by phlegmasia alba dolens of the right lower extremity on the tenth day postpartum. Four days later gangrene appeared, resulting in amputation two months later. Examination of the arteries in the amputated stump revealed thrombosis with endarteritic changes.

In Tate's⁶ report the gangrene involved both lower extremities and followed a severe attack of eclampsia. Death occurred twenty-three days later.

Schull's⁷ patient was a thirty-eight-year-old para vii who had 6 eclamptic seizures during labor. On the sixth day postpartum the left extremity became gangrenous. Death followed twelve days later with no autopsy.

O. Guthroff's⁸ reported 2 cases. The first was a twenty-two-year-old primipara who had 17 convulsions during labor. On the second day postpartum numerous areas of gangrene appeared on all extremities; the right foot was amputated two months later with recovery.

His second case occurred in a forty-seven-year-old para v who had numerous convulsions before and after delivery. She was out of bed on the tenth day; several

Gross pathologic examination revealed thrombosis of all large veins and arteries above the gangrenous area. Microscopic examination of veins revealed an extensive thrombophlebitis with periphlebitis.

On first analysis of the above case, it would appear that there is a very definite causal relationship between the administration of 32 doses of gynergin and the onset of the thrombosis. In 1930 P. Oginz² reported a case of puerperal gangrene following 42 doses of gynergin; however, his case had an associated severe puerperal sepsis in itself, a possible cause for the gangrene. E. J. McGrath³ reported the repeated production of gangrene in white rats by the administration of large doses of gynergin, the gangrene being due to intimal changes in the blood vessels with secondary thrombosis. Ergot similar to adrenalin stimulates the myoneural junctions of the sympathetic system, resulting in arterial contraction, its effect being less powerful but more enduring than adrenalin. Peripheral gangrene may result from the prolonged contraction of the capillaries or from thrombosis of larger vessels secondary to toxic intimal changes in their walls.

In the above case we have the presence of a definite thrombophlebitis in the limb affected by subsequent thrombosis for five weeks prior to the administration of the gynergin. The gangrene was localized to one extremity (which would be unusual for ergot poisoning) and the pulsations in the right extremity remained normal at all times. Also, the patient at no time evidenced any of the symptoms of the initial stage of ergot intoxication.

The findings of most significance, however, were the microscopic sections of veins removed from the upper portion of the amputated extremity. Many of these veins lying in close proximity to the larger arteries were filled with infected thrombi, with marked phlebitis and periphlebitis as evidenced by extensive polymorphonuclear infiltration.

The extension of the infection to the arterial walls by direct contiguity or via the vasa vasorum with secondary thrombosis would seem more plausible in view of the above, than to presuppose an atypical type of ergot poisoning plus an associated extensive thrombophlebitis.

CASE 2.—F. S., aged thirty-five, gravida iii, para ii. The first pregnancy terminated at seven and one-half months with the spontaneous delivery of a macerated fetus; etiology not definitely stated but thought to be due to a toxemia. Second pregnancy resulted in an uncomplicated spontaneous abortion during the third month.

Patient was admitted to hospital during the seventh month of her third pregnancy with a history of vomiting, frequent headaches, and edema of the ankles and face of one week's duration. She had had four generalized convulsions just previous to hospitalization. Examination revealed patient to be in a semicomatose condition; fundus was enlarged to the size of seven and one-half months' pregnancy and there was moderate edema of both lower extremities. Blood pressure was 145/100 and the urine contained a marked trace of albumin with many hyaline and granular casts. Shortly after admission she had another generalized convulsion.

A modified type of Stroganoff treatment was instituted. She remained in a semicomatose condition for twenty-four hours following which uterine contractions began. After a three-hour uneventful labor a macerated stillborn infant was delivered spontaneously. She improved rapidly following delivery and for seven days postpartum had no complaints. Temperature and pulse remained within normal limits. Blood pressure dropped to 130/80 and urine continued to show a trace of albumin. On the morning of the eighth day postpartum she began to complain of pain in the left lower extremity. This was relieved by $\frac{1}{2}$ gr. of morphine. Examination revealed no swelling or tenderness. She continued to have slight pain in the affected leg for the following three days. Temperature

The differential diagnosis between arterial thrombosis and embolism may be a difficult one. Emphasis is properly laid in the former upon the more gradual appearance of symptoms and in the latter upon the sudden onset and detection of some source for embolism especially cardiac disease.

CASE 3.—F. B., aged nineteen years, gravida iv, para ii. First two pregnancies terminated in normal spontaneous deliveries two and four years before admission. She had spontaneous uncomplicated abortion one year previously.

Last menstrual period had been three months previous to hospitalization. Chief complaint was vaginal bleeding of two days' duration associated with abdominal cramps. On admission bleeding was profuse; the uterus was enlarged to the size of a three months' pregnancy; and a 9 cm. fetus was found in the vaginal canal. Protruding from the cervical os was a piece of placental tissue which was removed. Bleeding was controlled with a vaginal packing. Twelve hours later her temperature rose to 102° F., so vaginal pack was removed. For the following five days temperature fluctuated between 100° to 104° F. associated with frequent chills. Only physical findings of note were moderate lower abdominal tenderness and a foul vaginal discharge. Examination of heart and lungs revealed no pathology.

Diagnosis, endometritis with thrombophlebitis of the placental site.

On the sixth day her temperature dropped to normal and remained there until discharge seven days later. On the seventh day following the abortion, she had slight swelling of the left ankle associated with tenderness. The day following discharge from the hospital she began to complain of pain in the left lower extremity in the region of the ankle and was re-admitted to the hospital. At this time the left foot and ankle were found swollen, reddened, and tender. Temperature was 103° F. and the white blood cells 30,000 with 84 per cent polymorphonuclears. The dorsalis pedis pulsations were identified.

It was now believed that the patient had an acute osteomyelitis secondary to a pelvic thrombophlebitis. Pain and tenderness persisted in the left foot for three days with no extension. X-ray revealed no pathology. The leg was elevated and wet dressings applied. On the morning of the fourth day following the onset of pain it was observed that the left foot and ankle were cold and cyanotic. The correct diagnosis was now apparent, namely, thrombosis, and amputation of the extremity was advised. The patient was transferred to another hospital where a midleg amputation was performed the following day, followed by an uneventful recovery. Unfortunately no pathologic examination of the amputated extremity was performed.

The presence of fever, pain, tenderness, and swelling in the region of the ankle with a palpable dorsalis pedis for three days previous to the onset of gangrene obviously rules out the possibility of embolism in this patient. The occurrence of arterial thrombosis in a patient previously suspected of having a phlebitis should point immediately to the correct diagnosis, namely, arteritis.

I wish to express my thanks to Dr. Charles A. Gordon, not only for permission to report the above cases but also for his many suggestions and kind assistance.

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hours later symptoms of arterial thrombosis in the left leg occurred. Gangrene resulted, with extensive superficial sloughing, followed by recovery.

In at least 6 more of the reported cases of peripheral gangrene, the presence of a pregnancy toxemia is strongly to be suspected. The frequent association of such a rare condition with eclampsia surely must be explained on some basis other than coincidence.

Dienst⁹ showed that the blood of eclamptic patients contained an excess of fibrin and fibrinogen, and Fahraens demonstrated the increased precipitation rate of the red blood cells; also an increase in the polymorphonuclear leucocytes and platelets has been demonstrated. We have ample evidence of the coagulation time being increased in the difficulties experienced in doing phlebotomies on these patients. Any or all of the above could be contributing factors in the formation of a thrombus, but they do not explain the production of a lesion of the intimal wall of the vessel so essential to the production of any thrombosis.

COMMENT

We have considerable evidence to show that the etiologic factor usually referred to as a toxin responsible for eclampsia is a specific circulatory poison, the hypertension which is such a constant finding being one of the manifestations of this intoxication. We know also that it has a direct effect upon the capillary walls, increasing their permeability, and Hinselmann¹⁰ has demonstrated the presence of an angiospasm in this condition. It is only a short step further to presuppose the occurrence of a toxic degeneration of the intima similar to that which occasionally occurs in typhoid, scarlet fever, and other severe intoxications, which plus the above mentioned blood changes would easily account for the thrombosis.

An interesting aspect of this case was the finding of all the symptoms of thrombosis, except gangrene, on the eighth day postpartum followed by gradual improvement until she was allowed out of bed on the twelfth day postpartum. At that time she had a recurrence of all the thrombotic symptoms, this time followed by the appearance of gangrene. Apparently thrombosis occurred during the first attack, but the collateral circulation was sufficient to prevent gangrene. However, allowing the patient to leave her bed so soon after the first attack resulted in an extension of the thrombosis with gangrene resulting. This assumption is borne out by the findings at operation. A well-organized thrombus was found in the popliteal artery with a more recent thrombus in the femoral artery. The occurrence of pain in the right leg with loss of popliteal pulsation three weeks following amputation of the left extremity also was undoubtedly due to thrombosis. Fortunately the collateral circulation was again sufficient to prevent gangrene.

In these patients the extent of the gangrene can never be predicted from the site of the thrombosis: closure of a large vessel in the thigh may only result in gangrene of a portion of the toe, whereas closure of a much smaller vessel at a lower level in a different individual may implicate the entire foot. The difference depends largely upon the efficiency of the collateral circulation and the rapidity of its development.

The performance of arteriotomy on this patient may be open to considerable criticism. To attempt this operation thirty-six hours after closure of the vessel alone will result in 100 per cent failures. Also the operation is only applicable to those cases where the intimal lining remains intact, i.e., in cases of embolism; and even in those cases if operation is not resorted to promptly, degenerative intimal changes will occur.

Arteriotomy in these cases of thrombosis, such as above described, will certainly not be successful due to the already existing lesion in the vessel wall which will cause a recurrence of the thrombosis following the arteriotomy.

Where there is reasonable doubt as to the etiologic factor, of course, the arteriotomy should be attempted, providing the diagnosis is made promptly.

cent. Smear revealed anisocytosis, poikilocytosis, many sickle cells, and an occasional normoblast. Moist preparation for sickling revealed approximately 50 per cent sickle cells. There was an increased resistance of red cells to hypotonic solutions. Icterus index 22. Serum bilirubin 1.5 mg. per 100 c.c. The Wassermann reaction was negative. Blood chemistry was within normal limits. Serum protein was 6.25 gm. per 100 c.c. with 2.60 gm. of albumin. Urinalysis: sp. gr. 1.014, albumin 3-plus, occasional pus and blood cells. Concentration and dilution tests showed maximum range of sp. gr. from 1.002 to 1.012. Phenolsulphonephthalein test (intravenous administration), 45 per cent excretion in two hours. Gastric analysis showed no free hydrochloric acid after Ewald test meal. Stool examinations were repeatedly negative.

Roentgenologic Studies.—Teleoroentgenogram of the heart showed definite cardiac enlargement. Total transverse diameter of heart was 15.2 cm.; internal diameter

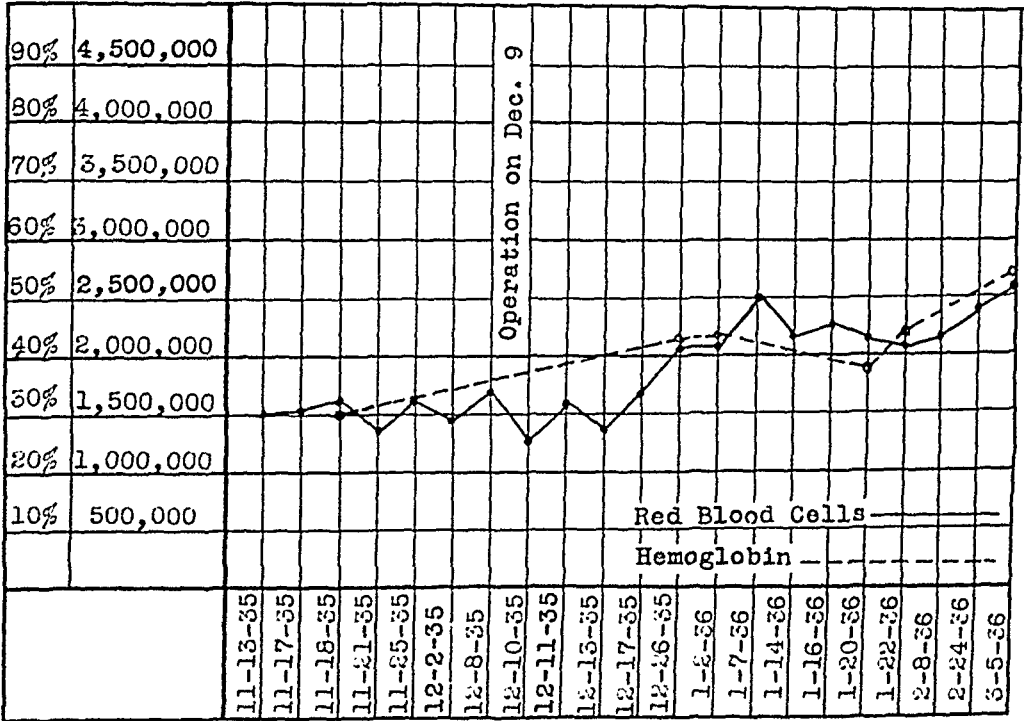


FIG. 1.—Graph of red blood counts and hemoglobin determinations (Sahli) throughout the period of observation.

of thorax was 23.7 cm. Films of the left hand and foot revealed mottled areas of decreased density in the ends of the metacarpals, the metatarsals and the phalanges. The midportions of the shafts of all bones appeared normal. A film of the skull showed mottled areas of decreased density throughout the vault, but chiefly in the parietal and frontal regions.

Course.—The patient was put to bed on a high protein, high caloric diet. Iron and ammonium citrate was given by mouth, and one ampule of liver extract was given intramuscularly daily. Although the patient's blood belongs in Group IV (Moss), on cross-matching 20 potential donors, no compatible one could be found. It was therefore impossible to give her a transfusion. The red count remained between 1,250,000 and 1,700,000 (see graph of blood counts). Termination of pregnancy was thought necessary, and hysterotomy with sterilization was selected as the method of choice. Operation was performed on Dec. 9, 1935. The postoperative

SICKLE CELL ANEMIA WITH PREGNANCY

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SICKLE cell anemia has figured largely in medical literature since Herrick¹ described the condition in 1910, and there have been many cases reported. Anderson and Ware,^{2,3} four years ago, published an excellent summary of the disease, presenting the cases observed at Grady Hospital up to that time. Sickie cell anemia with pregnancy is rare. Lash⁴ reported such a case in 1934, finding only two earlier ones in the literature. The following case seems to be the fourth.

REPORT OF CASE

A negro woman, aged twenty-five years, was admitted to the Obstetric Service of the Emory University Division of Grady Hospital on Nov. 13, 1935. Her last menstrual period had begun on Aug. 13, 1935.

History.—As a child the patient had been unable to carry on normal activity because of fatigue and shortness of breath on moderate exertion. Heart disease had first been diagnosed when she was ten. Two years later pain in both ankles had been severe enough to keep her in bed a week, although there was no swelling or fever. With limited activity she then became free of all symptoms until her marriage in 1931. During the next four years three pregnancies had terminated in abortions at four to seven months, the last of these occurring during an illness, said to have been pneumonia.

On Aug. 26, 1935, she was admitted to the medical outpatient department. A diagnosis of rheumatic heart disease was made and restriction of activity was advised. The patient returned on Oct. 19, 1935, complaining of shortness of breath and palpitation. Hemoglobin at this time was 40 per cent (Tallqvist); red cells numbered 1,590,000; white cells 20,000. Marked anisocytosis and poikilocytosis were observed. She was referred to the antepartum clinic because of amenorrhea for two months. There was no history of leg ulcers or abdominal pain. The family history was apparently irrelevant.

Examination.—The patient was well developed but undernourished. Her face appeared somewhat puffy. The conjunctiva and mucous membranes were extremely pale. Ophthalmoscopic examination was negative. Breast secretion was present. The left border of cardiac dullness was 11 cm. from the midsternal line in the fifth intercostal space. The right border of dullness was 4 cm. out in the fourth. No thrill was present. There was a diastolic shock at the base. The first and second sounds at the apex were clear and of good quality. There was a soft, blowing, systolic murmur at the apex transmitted to the base. The pulmonic second sound was accentuated. The radial pulses were equal, synchronous, and of good volume. The fundus uteri was palpable 5 cm. above the symphysis pubis. The liver and spleen were not felt. The cervix was softened. Goodell's and Hegar's signs were present. The uterus was symmetrically enlarged and softened. The extremities presented no scars or ulcers.

Laboratory Findings.—(Nov. 13, 1935.) Hemoglobin 45 per cent (Tallqvist); R.B.C. 1,500,000; leucocytes 26,800; neutrophils 80 per cent; lymphocytes 20 per

essentially the same. Serum albumin was 3.35 gm. per 100 c.c. There was a soft, blowing, systolic murmur at the pulmonic area. Persistent albuminuria, Grade 2 to 3, was present throughout the period of observation.

COMMENT

This case exemplifies the rather common error of mistaking sickle cell anemia for rheumatic heart disease. In addition it suggests an interesting line of supposition. Yater and Mollari⁵ mention the fact that two pregnancies in their patient had



Fig. 4.—Film of left hand which shows decreased density in the ends of the metacarpals and the phalanges.

terminated as abortions. Our patient had had three abortions and no full-term pregnancies. Sickle cell anemia as an etiological agent in habitual abortions is suggested.

It is well recognized that sickle cell anemia exists in both an active and a latent state, but the causes of exacerbations and remissions are not known. Since there was a definite remission following termination of pregnancy in this patient, the possibility exists that pregnancy was causing an exacerbation. Since pregnancy was not allowed to continue to a spontaneous termination, further cases must be studied before a conclusion can be reached.

The bone changes as shown by x-ray have been mentioned often.⁶⁻⁸ These are exemplified in Figs. 2 to 4.

course was uneventful. She was kept in the hospital for observation until Jan. 25, 1936, and when dismissed she was greatly improved. The patient was readmitted

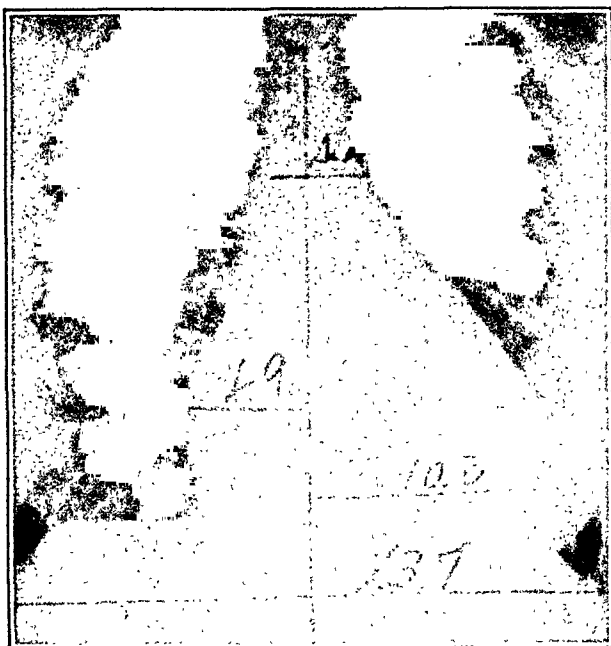


Fig. 2.—Photograph of teleoroentgenogram which shows definite cardiac hypertrophy, a typical feature of sickle cell anemia.

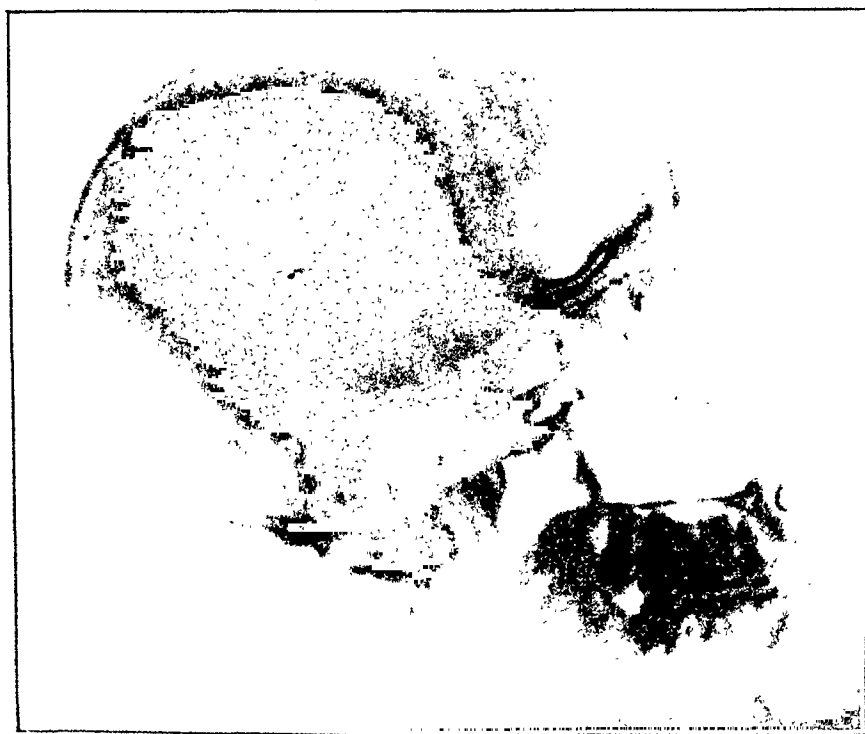


Fig. 3.—X-ray of skull showing mottled areas of decreased density throughout the vault.

for further study on Feb. 12, 1936. The red count at this time was 2,400,000 with hemoglobin of 40 per cent (Sahli). The phenolsulphonephthalein test revealed 85 per cent excretion in two hours. The concentration and dilution tests remained

CASE REPORT

History.—With the specimen the following data have been submitted to the laboratory: The patient is an American born, Jewish woman, aged thirty-four years. She has one child which is sixteen years of age. Thirteen and three years ago a cervical repair had been performed. She complained of dull pain in the back and lower abdomen which was gradually getting worse and was most marked during menstruation. The physical examination revealed a moderate tenderness in the lower abdomen, a slight enlargement of the uterus, and an induration and scarring of the vaginal portion of the cervix. A vaginal hysterectomy had been performed, from which the patient was recovering satisfactorily.

Gross Examination of Specimen.—The uterus and the left ovary were submitted for examination. The uterus measured 9 by 5 by 4 cm., its wall was 20 mm. thick and on the posterior surface of the fundus there was a circumscribed, subserous,



Fig. 1.—Four ray fungi in a small retention cyst of the cervix uteri. Note the accumulation of exudative cells about the fungi. Magnification $\times 100$.

grayish white node 20 mm. in diameter. The inner lining of the uterus was smooth and light yellow gray, and in the vaginal portion of the cervix several shallow, irregular depressions were found which radiated from the external mouth and alternated with tiny cysts which were filled by a mucoid material. The cervical canal was lined by an intact and pale mucosa. The ovary which measured 45 by 40 by 22 mm. contained a hemorrhagic corpus luteum and a small, thin-walled serous cyst.

Microscopic Examination.—The nodule of the fundus of the uterus proved to be a simple fibromyoma. The endometrium showed the changes of premenstrual hyperplasia. The cervix revealed a slight hyperplasia of the glands with cystic dilatation of some of the glands and a moderate periglandular fibrosis. In the vaginal portion of the cervix, closely adjacent to the surface epithelium and separated from it by a thin layer of connective tissue, there was a small cyst which was surrounded by accumulations of round cells and which was lined by an intact, low cylindrical epithelium with basal nuclei. The cyst was filled by a vacuolated, mucoid material

The question arises as to the presence and effect of renal disease in this patient. With no history of previous acute nephritis, a normal blood pressure throughout the period of observation, and improvement of phenolsulphonephthalein excretion with remission of the anemia, the probability is that the evidence of kidney disease is on the basis of the anemia. Nephrosis is to be considered.

SUMMARY

1. A case of sickle cell anemia complicated by pregnancy is presented.
2. Sickle cell anemia as a possible cause of abortions is suggested.
3. Pregnancy as a factor in exacerbations is considered.
4. This case is published with the hope that further cases will be studied to confirm or disprove the suppositions presented.

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ACTINOMYCOTIC GRANULES IN A RETENTION CYST OF THE CERVIX UTERI

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ACTINOMYCOSIS of the internal female sex organs is being reported with increasing frequency, and in the majority of the cases the lesions are found to affect the ovaries, fallopian tubes, and parametria. Most of the authors who have reviewed the literature or have described personal observations emphasize the great resistance of the uterus to the infection, stating that if the uterus does become involved it is due to the extension of the process from the parametrium (Nürnbergger,¹ Daniel and Mavrodin,² Cornell,³ and others). The actinomycosis of the ovaries, tubes, and parametria is usually secondary to an infection of the intestine, particularly of the cecum or appendix. From the intestine the infection spreads to the ovaries and parametrian tissue either retroperitoneally or intraperitoneally along pericecal or periappendiceal adhesions. Blasek⁴ has pointed out that the actinomycotic infection may progress while the primary lesion at the point of entrance in the intestine heals. It requires then a very careful histologic examination in order to detect the residues of the initial lesion in the intestine. Daniel and Mavrodin² refer to the external genitalia as a possible port of entrance of the infection.

From time to time, however, cases are described which suggest that the ray fungus may directly infect the internal female genitalia, the primary lesion being located in the uterus. With regard to this primary actinomycosis of the uterus, an observation is of interest which I have recently made and which indicates that the infection may remain dormant.

affinity to the acid stains (Fig. 2). Some of the protrusions were enclosed in the large multinuclear cells and showed evidence of disintegration (Fig. 3). In sections stained after Gram-Weigert the central portion showed branched and segmented filaments which were thicker than those commonly seen in actinomyotic granules. The filaments contained tiny, spherical bodies which stained deeper than the surrounding structures. There were small crevices in the center of the bodies in which flattened leucocytes were located.

When the ray fungi were discovered in the subepithelial cyst, serial sections were made from the remaining portion of the paraffin block and numerous sections were taken from the cervix, but no other bodies could be detected.

DISCUSSION

The identification of the granules in the small cyst of the cervix as actinomyces rests entirely upon their morphology since no cultures were made from the content of the cyst. The structure of these granules is so typical that they undoubtedly belong to one of the varieties of actinomyces which, in living tissue, form club-shaped thickenings of the free ends of the mycelia. In all the cases of actinomycosis of the uterus described in the literature the diagnosis was based upon the demonstration of the characteristic bodies either in sections or smears.

A structure which can be confused with actinomyces is the actinophytic evolution form of certain bacteria, notably staphylococci (Botryomyces). In chronic suppurative osteomyelitis the staphylococci form occasionally compact clumps which are surrounded by a homogeneous shell. Berger, Vallée and Vézina⁵ have recently described a staphylococcic actinophytosis of the vulva. It is, however, only under low power magnification that the staphylococci granules can be mistaken for actinomyces, since the finer morphology is different, the former being composed of cocci, the latter of branched filaments.

How does the actinomyces gain entrance into the uterus? In order to infect the actinomyces must find a break in the continuity of the tissues. The case of Giordano which is often quoted in the literature concerns a woman, aged sixty-four years, who used to feed her chickens with grain. Her uterus was prolapsed and on the posterior lip of the vaginal portion of the cervix there was a small, indurated area. The external uterine orifice was half open and the cervical canal contained thick cloudy fluid in which the characteristic sulphur bodies were suspended. Vaginal hysterectomy was followed by complete recovery. Giordano suggests that the spores of the fungus were present in the grain used for feeding the chickens and that they might have settled on the eroded and prolapsed cervix of the uterus. This is the only case in which the patient had anything to do with grain. In two instances the actinomycosis of the uterus followed an instrumental abortion (Haselhorst⁷ and Junghans⁸). In Haselhorst's case a fistulous tract extended from near the internal uterine orifice into the left parametrium which was the site of a sclerosing, suppurative inflammation involving the left tube, the sacral bone and the fifth lumbar vertebra. Junghans' case showed an instrumental perforation in the anterior fornix of the vagina from which the actinomyotic infection seemed to have taken its origin. In the cases described by Barth⁹ and Tietze,¹⁰ the infection was traced to ulcerative lesions caused by intrauterine, contraceptive pessaries. In the cases of Mitra¹¹ and Christeller¹² the mode of infection is obscure.

In the case which I have described it is possible that the fungus may have been inoculated into the cervix during the repair performed three years previously. The spores of actinomyces are much more widely distributed than formerly assumed. The fungus is either of low virulence or the resistance of the tissues is strong enough to prevent the spreading of the infection. In favor of the later explanation is the finding of regressive changes of the mycelia and especially the phagocytosis of the

which contained large, multinucleated cells with vacuolated cytoplasm and polymorphonuclear leucocytes. The cyst also contained four roundish bodies which measured 100 microns in diameter and were surrounded by accumulations of leuco-

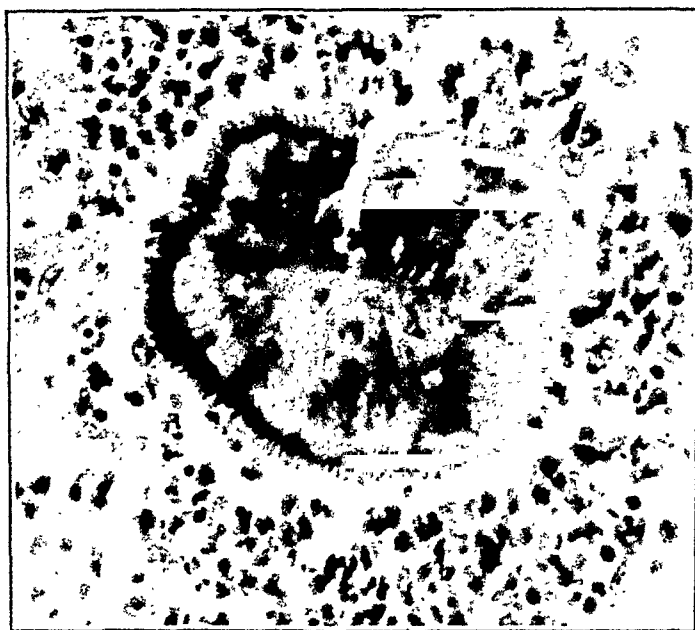


Fig. 2.—Ray fungus surrounded by pus cells and macrophages. Magnification $\times 600$.



Fig. 3.—Phagocytosis of the club-shaped endings of the mycelia by multinucleated macrophages and disintegration of the mycelia in the cytoplasm of these cells. Magnification $\times 1000$.

cytes and multinuclear cells (Fig. 1). These bodies consisted of a homogeneous center and a peripheral zone of regular, club-shaped protrusions which had a great

On admission the temperature was 100.8° F. by mouth, the pulse rate 106, and respirations 34. She was rational and not excited, she answered questions readily and intelligently.

There was a soft, blowing systolic murmur which was best heard at the apex. The heart rate and rhythm were regular, and there was no apparent cardiac enlargement. The blood pressure was 136/70.

The abdomen was moderately distended. It was believed that peristaltic activity could be seen in the upper left quadrant. There was some left-sided tenderness and also some rigidity of the left abdominal muscles. The degree of rigidity was difficult to determine. The uterus was enlarged to the size of a normal seven months' pregnancy, but the fundus was high and lying definitely to the right in the upper abdomen. There was also evidence of intestinal distention. No peristaltic action was audible on auscultation.

On bimanual examination the head of the child was found to be at the entrance of the birth canal but was not engaged.

Preoperative Treatment and Course.—A presumptive diagnosis of intestinal obstruction had been made by Dr. C. H. Bair, the attending physician, and the



Fig. 1.—Photograph by Dr. E. L. Saylor showing dilatation of sigmoid colon.

history, along with the evidence found on physical examination, strongly supported this possibility, but it was difficult to determine the source of the intermittent pains as the fever suggested some type of infection with premature labor pains. Accordingly, it was decided best to treat the patient conservatively with continuous duodenal drainage by the use of the Wangenstein apparatus.

A soap-suds enema given one hour after admission returned clear, and a moderate amount of flatus was expelled. Despite the fact that the patient complained of severe pain, opiates and other sedatives were withheld. Water was given freely by mouth and removed through the drainage tube.

Eight hours later the clinical condition was unimproved, and it was evident the drainage apparatus was not relieving the distention. In fact, the abdomen was definitely more rounded and tense. The temperature had risen to 102.6° F. and the pulse rate to 118. One thousand cubic centimeters of normal saline were given intravenously. A blood sugar reading revealed 122 mg. per 100 c.c. After a second consultation, it was decided that immediate operation was advisable.

Operative Procedure and Findings.—The operation was carried out twelve hours after admission under nitrous oxide, oxygen, and ether. A left paramedian incision was made from 5 cm. above the umbilicus to a point near the pubic symphysis. Up-

mycelia by multinucleated macrophages in the cytoplasm of which they disintegrate. That the granules did produce some irritation is shown by the accumulation of pus cells and macrophages about the granules and the round cell infiltrations which are confined to the vicinity of the cyst which contains the granules. Thus the case may be considered as morphologic confirmation of the high resistance of the uterus to infections with the ray fungus.

SUMMARY

In a small retention cyst of the uterine cervix typical actinomycotic granules were found incidentally. The infection was well localized and did not show any evidences of progression. These findings seem to illustrate the high resistance of the uterus to the infection with the ray fungus.

The literature on primary actinomycosis of the uterus is discussed briefly.

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LATE PREGNANCY COMPLICATED BY INTESTINAL OBSTRUCTION DUE TO AN OPENING IN THE MESENTERY IN A YOUNG PRIMIPARA

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INTESTINAL obstruction due to a loop of bowel becoming strangulated in a congenital opening of the mesentery is rare. The following is a report of such a case occurring in a young primipara seven months pregnant, in which it was quite difficult to differentiate the pain due to possible bowel obstruction from that due to premature uterine contractions.

The patient, a white primipara, aged twenty-one, seven months pregnant, entered the City Hospital of Akron at midnight, April 19, 1936. Her chief complaints on admission were severe cramplike pains over the entire abdomen and marked nausea with vomiting. She had been ill for about ten hours. The onset had been rather abrupt with increasing severity of the symptoms. She had had no bowel movements subsequent to the onset but she did recall passing some flatus. About four to six hours after the onset of the illness she began to feel quite distended.

There was no history of surgical operation in the past and no other essential history was elicited. A white blood count showed 20,000 leucocytes with 62 per cent polymorphonuclears. The urine showed 2-plus sugar with 3-plus acetone bodies and many pus cells.

Physical Examination.—The patient was a well-nourished young woman, lying in bed and appearing quite ill. Her respirations were increased and she seemed to have attacks of cramplike pain in the abdomen, coming on intermittently about every three to four minutes.

travenously. At 9:00 P.M., pitressin 1 c.c. and morphine, gr. $\frac{1}{4}$, were given. At 9:15 P.M. the patient had an involuntary bowel movement consisting of a moderate amount of liquid feces.

Postpartum Course.—On April 22 the Wangenstein apparatus was still in use. One cubic centimeter of pitressin was given every four hours for six doses. Sodium luminal, gr. ii, was given as a sedative and the patient was allowed tea and ice chips. Between 1:00 A.M. and 8:00 A.M. the patient had four involuntary bowel movements of liquid stool. The uterus was firm, the lochia normal, but the abdomen appeared to be slightly distended. During the evening the patient felt well enough to read for about an hour.

The Wangenstein apparatus was discontinued. At 8:00 P.M. the patient was given a glass of milk and 3 gr. of sodium oral, and at 8:15 P.M. there was a voluntary stool which was of liquid to soft consistency.

On April 23 the patient had slept fairly well but awoke with a somewhat rigid abdomen and a rectal tube was inserted for relief. Patient was given a liquid diet on this day. There was a normal bowel movement in the morning and an involuntary one at 5:30 P.M. The day was otherwise uneventful. The temperature ranged from 99 to 100.4° F.

Her general condition now began to improve rapidly. On April 24 she received a soft diet. No more involuntary bowel movements occurred. On April 26 the skin clips and retention sutures were removed and the temperature and pulse rate reached normal. On April 28 the abdominal wound gave way in the lower portion. The wound edges were separated and a quantity of foul-smelling pus escaped. A rubber tissue drain was inserted temporarily into the wound to aid the drainage.

The patient was placed on a regular diet April 29. The remaining course in the hospital was uneventful. The wound infection cleared up rapidly and on May 8 the patient was discharged in very good condition.

The baby weighed 3 pounds, 4 ounces at birth. She was taken direct to the incubator and received formula feedings by gavage and infusions of 5 per cent glucose in normal saline, 60 c.c., for the first two weeks. On June 9, 1936, she weighed 5 pounds, 1 ounce and at the time this is written, is in her twelfth week in good condition.

Béclère, C.: The Passage of Lipiodol Into the Tubes and Into the Peritoneal Cavity. Has It Dangers? Bull. Soc. d'obst. et de gynéc. 25: 449, 1936.

During the past ten years the author has performed more than 800 hysterosalpingographies. He has also performed the test on 220 women who had uterine hemorrhage, and he has never observed any accidents as a result of this, except in one case where salpingitis occurred. The author is firmly of the belief that the spill of lipiodol into the peritoneal cavity has absolutely no danger. Even where there is a chronic infection of the genitalia and in the uterine cavity itself, it is astonishing how remarkable is the lack of peritoneal reaction from this procedure. On the other hand, the passage of lipiodol into the tubes does carry some risk with it. In about 1 per cent of the cases a salpingitis flares up. This, however, occurs only in cases of cystic salpingitis. The discovery of cystic salpingitis by means of hysterosalpingography has been a revelation to the author. In 66 cases of sterility examined by this procedure, he found cystic salpingitis in 30 per cent. Also, in a series of 75 cases with uterine hemorrhage of unknown origin, the author found cystic salpingitis in 20 per cent. Contrary to many authors, Béclère is of the opinion that uterine hemorrhage of unknown origin is not a contraindication to injection of lipiodol into the uterine cavity.

on opening the peritoneum quite a large amount of cloudy, seropurulent fluid was found which was removed by suction. The enlarged, gravid uterus and the greatly distended loops of bowel made exploration exceedingly difficult.

A circular opening with rigid walls, which easily admitted two fingers, was found in the mesocolon of the sigmoid near its midportion, and a loop of redundant sigmoid had passed through the aperture, becoming firmly incarcerated and obstructed. All of the colon proximal to the obstruction was distended and filled with gas and large soft masses of fecal material. Two loops of bowel directly involved at the site of the obstruction were dilated to about six inches in diameter. This extreme colonic distention pressed upward against the diaphragm forcibly and extended from that region downward into the culdesac space posterior to the uterus. The enlarged uterine fundus was pushed far to the right and all of the available abdominal space was occupied by the viscera under the utmost pressure.

A rectal tube was inserted during the operation in an effort to collapse the affected sigmoid but without success. A trocar was then thrust through the distended colon and the compressed gas and fluid contents were removed with resulting collapse of the bowel. Contamination was controlled by a purse-string suture at the site of the puncture and the bowel carefully closed with intestinal catgut. The obstructed portion of the bowel was freed from the hole in the mesentery and with the exception of one questionable area on the antimesenteric aspect of the loop, which had been strangulated, the bowel appeared in good condition. Because of the generally unfavorable condition of the patient, nothing further was done. The incision was closed without drainage.

Postoperative Treatment and Progress.—The patient was given 1,500 c.c. of 5 per cent glucose in normal saline intravenously and external heat was applied. Surgical pituitrin was withheld for fear that uterine contractions would result. A rectal tube was introduced and colonic irrigations with warm normal saline were carried out. The returns were colored but no fecal material appeared.

The perineum was prepared for a possible inevitable premature delivery and the Wangenstein apparatus was again inserted. The temperature ranged from 100.2° F. to 103.6° F. and the pulse rate from 115 to 128. A culture from the abdominal fluid taken at the time of operation revealed no bacteria to be present. On April 20 the patient slept well when undisturbed by the irrigations, the returns of which were light brown in color. A few small flakes of fecal material appeared on this date. Morphine sulphate, gr. $\frac{1}{4}$, was given twice on this date for pain, and 1,500 c.c. of 5 per cent glucose in normal saline solution was given intravenously twice daily. The temperature and pulse rate remained about the same. On April 21 the patient passed a large amount of brown liquid stool at about 4:30 A.M. and was placed on a liquid diet.

At about 1:30 P.M. the patient's membranes ruptured spontaneously. Rectal examination revealed the cervix to be about $1\frac{1}{2}$ cm. dilated. The patient was transferred to the maternity division where she began having acute labor pains about forty-five minutes after the membranes had ruptured. A scultetus binder was firmly applied. At 2:15 P.M. a bloody show appeared and the pains became more severe. At 3:00 P.M. rectal examination showed 4 cm. dilatation and the cervix was thinning. Dilatation was complete at 3:30 P.M., and the patient was taken to the delivery room where she spontaneously delivered a living, premature baby girl at 4:30 P.M. The placenta was expressed by the modified Credé method at 4:55 P.M. and found to be complete. Infundin, $\frac{1}{2}$ c.c., was given subcutaneously at this time.

After delivery a rectal tube was reinserted, the abdominal binder applied, and the patient was moved to her room. The temperature ranged from 102.4° to 102.8° F. and the pulse from 90 to 120 on this date. At 8:00 P.M. she received 1,500 c.c. of 5 per cent glucose in normal saline with 10 c.c. of calcium lactogluconate, in-

on speculum examination revealed to be eroded, cystic, and had a small cervical polyp protruding from external os. Uterus was well anterior but the size could not be made out. No masses or tenderness was felt in either fornix.

Operation.—Laparotomy two hours after admission revealed the following: The peritoneal cavity was filled with free and clotted blood, and after removal of some

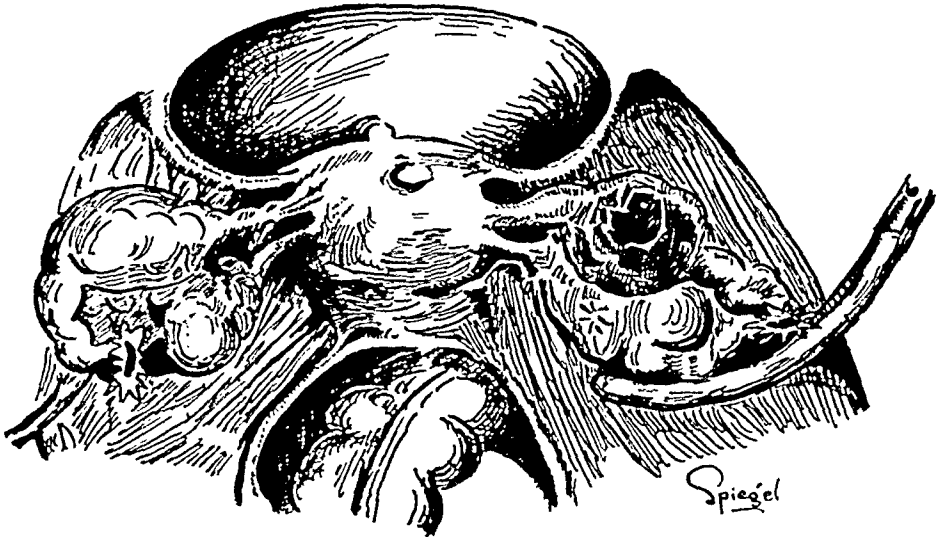


Fig. 1.—Schematic drawing of ruptured right tubal pregnancy and unruptured left.



Fig. 2.—High powered microphotograph of left tube, showing young edematous chorionic villus within the lumen. The wall lining the lumen is composed of decidual cells.

of the clots the left adnexa appeared to be normal to the examining hand, but the right tube was felt to be ruptured. The right tube and ovary were removed. The uterus appeared definitely larger than normal and two small fibroids the size of a hazelnut were on the anterior wall of the uterus. These were enucleated and the rent was closed over by interrupted chromic No. 2 sutures. Inspection of the left side immediately before closure revealed a dilatation in midportion of the tube which

BILATERAL SIMULTANEOUS TUBAL PREGNANCY

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(From the Obstetric and Gynecologic Service of the Beth-El Hospital)

BILATERAL simultaneous tubal pregnancy is infrequent enough and at times might be elusive enough to justify the report of this case. When the calamity occurs in tubal pregnancy, laparotomy and ligation of bleeding vessels is of paramount importance and when this is done, examination of the opposite adnexa is equally if not more important. As will be shown later, the unruptured tube on palpation, at the outset was considered normal, but actual visualization before closure revealed another tubal pregnancy, which if overlooked might have proved very unfortunate to the patient and embarrassing to the operator.

The presence of a bilateral corpus luteum leads one to doubt whether the cyclic maturation of one follicle is the accepted order. Here both ovaries had corpora lutea present, and undoubtedly the maturation of two follicles had taken place; two ova were extruded and each probably fertilized in their respective tubes, and there arrested to give us this rare condition of bilateral concurrent tubal pregnancy. The only other condition which might account for this is superfetation, which would be difficult to prove. Suffice it to say however, that the pathologic report does not substantiate the presence of embryos of different lengths of gestation.

Siegler reported a case in which one side had a ruptured tubal pregnancy, while the opposite side showed evidence of a tubal abortion. He reviewed the literature and, although the first case was reported in 1890, only 16 authentic cases were found to be on record according to Schochardt, quoting Cheval, who reported another case in 1928. In 1931 Meyer found that there were 28 authentic cases. Another case was reported as recent as 1932, by F. D. Johnson.

Case Report.—Mrs. L. M. (Hospital number 72002), white, thirty-six years old, admitted to the service of Dr. Oginsz, complaining of fainting spells, pain in lower abdomen, and prolonged scanty menstruation. She was married thirteen years, had 2 spontaneous deliveries, twelve and eight years, respectively. She had had three induced abortions since her last delivery, the last one four years ago and all were uncomplicated. Catamenia set in at twelve years of age, regular every twenty-eight days and of three days' duration. Her last regular menstrual period was June 22. On July 20 when the period was expected she began to bleed rather scantily and continued to bleed until two days before admission when she passed a large clot. On the day of admission, Aug. 7, 1935, she experienced dull pain in the lower abdomen and had two fainting spells. During admission to the hospital the admitting physician noted another fainting spell and she fainted again one hour later while in bed. During the last fainting spell she was cold and clammy and there was a decided drop in her blood pressure. The above history was sufficient to lead one to the inevitable conclusion of a ruptured tubal pregnancy for the physical examination was of very little value.

Laboratory Findings.—R.B.C. 3,900,000, Hemoglobin 88 per cent, W.B.C. 12,500 with 82 per cent polymorphonuclears and 18 per cent mononuclears. The blood pressure was 120/84. The urine was negative.

Physical Examination.—An adult female seen on admission not acutely ill and of fair complexion with moderately rapid pulse. Abdomen moderately obese, tender in lower right side, no Cullen's sign present. Vaginally there was a multipurulent, thick purpurulent vaginal discharge. Cervix tender to touch and

Right tube was dilated about 3 cm. from fimbria. The serosa was dark red, wall was thin and ruptured in the dilated area with blood clot in which were present chorionic villi. No fetal parts were found.

Right ovary had a corpus luteum 10 cm. in diameter. The 2 fibrous tumors each 1 cm. in diameter presented interlacing whorls of fibrous tissue.

Microscopic Findings.—Section of right tube showed layers of the tubal wall completely disoriented by edema, congestion, and infiltrated by numerous masses of trophoblasts. The tube proximal to the area of gestation showed edema, congestion, and leucocytic infiltration but no evidence of previous chronic infiltration. Section of right ovary showed a large vascularized corpus luteum and an occasional follicular cyst.

Section of left tube showed the lumen occupied by numerous chorionic villi; the mucosa had been replaced by a thick zone of deciduoid cells. The tubal wall was intensely edematous, congested, and diffusely infiltrated with small round cells and polymorphonuclear leucocytes. Section of tube proximal to site of gestation showed no evidence of chronic infiltration.

Diagnosis.—Right tubal gestation ruptured, left tubal gestation unruptured, and right corpus luteum vera.

The postoperative course was rather stormy. Immediately after the operation she became markedly distended and the distention was limited to the upper abdomen. On the fourth postoperative day, during the expulsion of an enema, she suddenly felt a puffing up of the left labia, which soon became ecchymotic and swollen. This was later determined to be a ruptured varix in the left vulva. After applying pressure and cold packs to that area, the bleeding was controlled and ecchymosis spread to the opposite side down the buttocks and to the left groin and lower portion of the abdomen. On the day of discharge the ecchymosis had entirely disappeared.

On the eighth postoperative day, the patient emaciated and was taken to the operating room and the abdominal wound resutured. For two days after the resuturing of the abdominal wound, distention continued and was combated by enemas, rectal tube, and pituitrin. After that the postoperative course was uneventful. The patient was discharged on the twenty-fourth day after the operation, and at that time the abdominal wound was intact and firm throughout. The ecchymosis from the ruptured varix had almost entirely disappeared. Vaginal examination revealed the cervix high in the vagina and freely movable. The uterus was found in normal position and both fornices were normal.

1363 EASTERN PARKWAY

Yamabe, A., and Yun, T. W.: A Case of Spina Bifida Diagnosed During Pregnancy, *Jap. J. Obst. & Gynec.* 19: 119, 1936.

In a case of hydramnios the authors could not make a diagnosis of fetal presentation. They, therefore, took an x-ray picture and were surprised to find a case of spina bifida. After delivery they verified the diagnosis. They emphasize the necessity of taking x-ray pictures in all cases where malformations of the fetus are suspected but not diagnosed for certain.

J. P. GREENHILL.

LEVINE: BILATERAL SIMULTANEOUS TUBAL PREGNANCY

was concluded to be another tubal pregnancy. The ovary on that side showed the presence of a recent corpus luteum. The left tube was removed, leaving the ovary in situ. The abdomen was closed in layers.

Pathologic Report.—Specimen consisted of 2 fallopian tubes, right ovary, and two small fibrous tumors. The left tube was dilated 5 cm. from the fimbriated

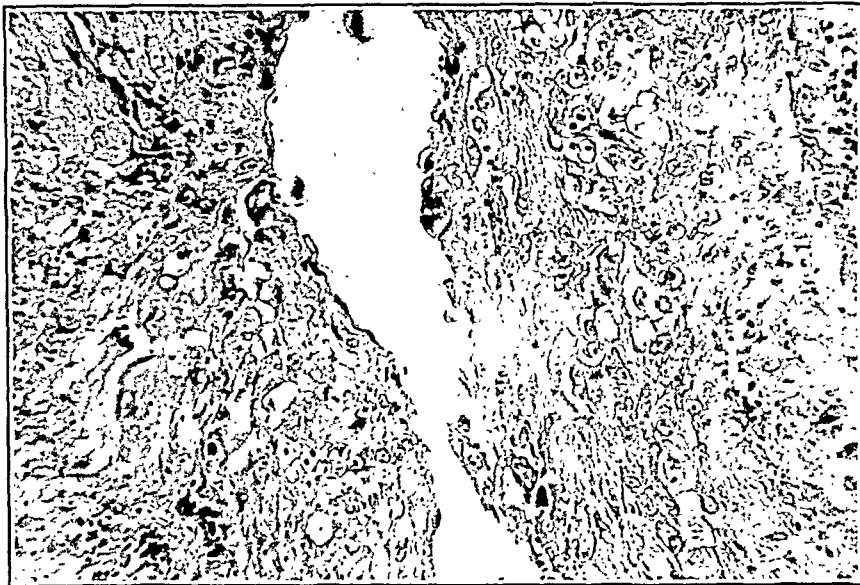


Fig. 3.—High powered microphotograph of right tube, showing the wall lining the lumen entirely converted into decidual tissue. Note the irregular character of the decidual cells.

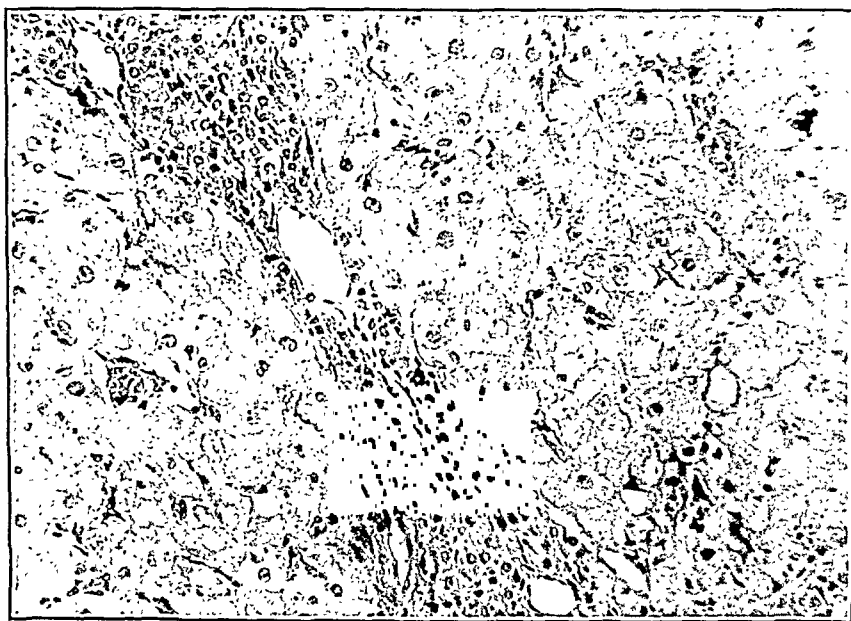


Fig. 4.—High powered microphotograph of right ovary, showing a part of its contained corpus luteum vera.

end to diameter of 2 cm.; the serosa was dark red, glistening, no rupture. Sections showed thin tubal wall with lumen filled completely by chorionic villi within which was a complete amniotic sac which contained a tiny curled wormlike embryo 2 cm. and $\frac{1}{2}$ mm. across. The mesosalpinx in relation to this part of the tube contained dark hemorrhagic material.

Patient was admitted to the Beth-El Hospital on Aug. 26, 1935. Lungs were negative. Heart presented a systolic murmur at apex and slight tachycardia. General examination otherwise negative.

Abdominal Examination.—Relaxed abdominal wall. Midline scar of previous operation. Fundus palpable two fingerbreadths above the symphysis. Above the fundal mass, another mass the size of a large orange was palpable, with smaller masses transversely across to the right side. These were freely movable with a sense of hardness like that of small parts. No fetal heart sounds were heard.

Vaginal Examination.—There was visible vaginal bleeding. Cervix high and in the axis of vagina. Abdominal mass was movable with the cervix. Fornices were negative. Uterus could not be mapped out definitely.

The Friedman test was done on August 27 and reported negative on Aug. 29, 1935.



Fig. 1.

X-rays were taken on August 27 and on August 30, with following findings: "Fetus lying transversely across the abdomen with head on the left side anteriorly, with the fetal spine almost at right angle to the maternal spine. There is no definite evidence of overriding of the skull bones. It appears to be extrauterine." (Fig. 1.)

Hysterography was performed by injecting 15 c.c. of lipiodol into the uterus and x-rays taken, one after injection of 10 c.c. of lipiodol and another exposure after the full amount. A third exposure was taken after the removal of the cannula.

Hysterography showed on first exposure filling of uterus and part of left tube and second exposure showed complete filling of the tube and irregular filling of the uterine cavity, not reaching above the pubes (Fig. 2).

The diagnosis of extrauterine pregnancy was thus confirmed.

Laparotomy was performed on Aug. 30, 1935, under spinal anesthesia. A seven months' macerated fetus was found free in the abdomen. Membranes were ruptured, there being no evidence of liquor amnii. A large placenta was found resting on top of the uterus, the concavity of the placenta resting over the convexity of the

ABDOMINAL PREGNANCY. DIAGNOSIS CONFIRMED BY HYSTEROGRAPHY*

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ALTHOUGH hystero-graphy has been used for many purposes in gynecology, a careful search of the literature reveals but seven reports where this method was used to aid a diagnosis where abdominal pregnancy was present.¹

Mrs. R. R., white, housewife, aged thirty-four years, para i, gravida vi, presented herself for prenatal care in the fourth month of gestation. Last menstrual period was on Dec. 6, 1934; the date of expected delivery was Sept. 12, 1935.

Menstruation began at the age of twelve years, normal in type. Patient had been married twelve years. Husband contracted a neisserian infection seven years ago, which was apparently transmitted to the wife, who gives a history of pelvic inflammatory disease shortly after this. Patient has one child living and well, aged ten years. This was a spontaneous delivery with normal puerperium.

She had had one spontaneous abortion and two induced abortions with no apparent sequelae.

Six years ago patient had a tubal gestation, at which time a right salpingo-oophorectomy and appendectomy were performed. She had an uneventful recovery and was discharged from hospital on the fourteenth day.

Patient reported for examination every three weeks. The first visit was made in March, 1935, when she gave a history of having pain in the abdomen for the past eight weeks with slight bleeding from time to time.

She had previously been attended at another clinic, where she was informed that it would be advisable for her to undergo laparotomy for the investigation of her pain and bleeding.

Examination revealed the fundus to be increased in size and exhibiting all the signs of a four months' gestation. There was no bleeding and no pain at this time.

Urinalysis was negative throughout and blood pressure within normal limits. Weight increase was steady and constant until the seventh month of gestation, when she lost weight rapidly and consistently.

On June 15, 1935, the fetal heart was heard at the median line above the umbilicus, and the outline of ovum appeared normal for this stage of gestation.

On July 25, 1935, patient complained of not having felt fetal movements and the heart could no longer be heard. No change in the size, shape, or consistency of ovoid was observed at this time.

On Aug. 8, 1935, patient was again examined. Fetal heart was not heard. There was no pain or bleeding, but persistent loss of weight.

On Aug. 22, 1935, she had a slight bloody discharge from the vagina. At this examination the fundal mass was palpable below the umbilicus and was the size of a four months' gestation. The fetus was movable above the fundal mass. These findings gave the impression of abdominal pregnancy with dead fetus, and the patient was ordered to the hospital.

*Presented at a meeting of the Brooklyn Gynecological Society, November 6, 1936.

Follow-Up.—On Nov. 6, 1935, six weeks after operation, patient exhibited a persistent vaginitis and evidence of climacteric changes. Treatment for vaginitis instituted. Abdominal scar was firm, dry, and clean.

On Nov. 22, 1935, vaginitis was much improved and her general condition was very good.

On Dec. 20, 1935, vaginitis had entirely cleared up and her general condition was excellent. The abdominal scar was firm, with no evidence of herniation. Patient discharged.

COMMENT

This extrauterine pregnancy evidently resulted from a second ectopic following the first which was in the right tube. It aborted through the left tube and found its nidation at the fimbriated end of the left tube, as shown by the firm attachment to the placenta. This calls to our attention the fact that where there has been an ectopic on one side following neisserian infection, there is the possibility of another ectopic occurring in the opposite tube.

The suspicion of extrauterine pregnancy was aroused by the patient's symptoms of pain and some bleeding during the first two months of gestation, but diagnosis could not be established as long as the membranes were intact and the fetus confined to the amniotic sac, giving the impression of intrauterine pregnancy. After the rupture of membranes and cessation of fetal heart, diagnosis of extrauterine pregnancy was immediately suspected.

While the flat x-ray plate showed the fetus lying transversely, it still did not absolutely exclude an extrauterine pregnancy. The use of hystero-graphy, however, definitely confirmed our impressions.

220 NEW YORK AVENUE

A GIANT OVARIAN CYST

CHARLES G. STRICKLAND, M.D., ERIE, PA.

(From the Hamot Hospital)

ON JULY 8, 1936, there was admitted to Hamot Hospital a patient with a giant ovarian cyst. Measured by most conservative standards this tumor, as seen first, must have weighed 160 pounds and probably ran considerably over that figure. The patient, an Iroquois Indian, was a married woman of thirty-four years, who had one normal child seven years old. About thirty months prior to admission her abdomen began to increase in size. At first she deemed herself pregnant but after nine months had elapsed, during which time she had regular periods, the patient consulted a physician who told her that the supposed pregnancy was an ovarian cyst. This woman was a sincere Christian Scientist and, as a result, not only refused the surgical relief offered at that time but so far as is known was treated only by Christian Science practitioners from that time until her hospital admission. Her tremendous size, her obvious distress, and her profound weakness at last drove her to the hospital. For the sake of brevity, only essential points will be mentioned in the following physical examination.

An emaciated woman with tremendous overdistention of the abdomen and in obvious distress. She was orthopneic and showed marked edema of both legs. Her height was 5 feet, $3\frac{1}{4}$ inches and her weight 296 pounds. (Her normal weight had been 150 pounds.) The superficial veins of the neck were engorged and the whole

uterus, as is clearly shown in the photograph. The fimbriated end of the left tube was adherent to the placenta. A portion of placenta was attached to the left broad ligament. Part of the membranes were found attached to the small intestine and postparietal peritoneum and these were left in place.

Resection of the broad ligament and left tube together with fixation of the uterus was done. The right tube and ovary missing, removed at previous operation. Abdomen was closed in layers in the usual manner.



Fig. 2.

Laboratory Findings.—Urinalysis was negative throughout stay in hospital. Blood pressure within normal limits, and blood count was as follows: Erythrocytes 4,200,000, leucocytes 9,200, hemoglobin 85 per cent, polymorphonuclears 71 per cent, and monocytes 29 per cent.

Patient was out of bed on the fourteenth day and discharged on the seventeenth day in good condition. Wound healed by primary union. Bimanual examination on discharge showed fundus anterior, fixation holding, no masses and no tenderness.

In spite of our best efforts, including considerable stimulation and many glucose transfusions, the patient progressively lost strength and died August 21 in an attack of acute pulmonary edema. The weight of the patient six days before death was 160 pounds. At no time was she considered even a fair risk for surgery nor do I personally believe that she could have survived surgical procedure at any time subsequent to her admission.

A postmortem examination was done. The tumor was a pseudomucinous cystadenoma of the right ovary. The rest of the pelvic organs were normal. The cystadenoma had two large compartments containing $7\frac{1}{2}$ gallons or 71 pounds of fluid. The cyst wall was lightly adherent to the abdominal wall probably as a result of the tapping but elsewhere free. The cadaver after removal of the tumor weighed 93 pounds. The sac of the tumor weighed 4 pounds. Microscopic findings were typical ones of a pseudomucinous cystadenoma. The cyst fluid was dark brown in color and the consistency of a thin syrup. The specific gravity was 1026 and the reaction slightly alkaline. It contained 3.8 per cent albumin but no sugar. All specimens including those from theappings were sterile.

This case is reported because apparently it exceeds in size any recently noted.

153 WEST SEVENTH STREET

CONGENITAL HYDROTHORAX

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BALLANTYNE has defined general fetal edema as "a morbid condition of the fetus characterized by general anasarca, by the presence of fluid effusions in the peritoneal, pleural, and pericardial sacs and usually by edema of the placenta." The disease is uncommon yet adequately represented in the literature in the writings of Ballantyne and Schumann. Congenital hydrothorax (bilateral) entirely dissociated from hydrops universalis is rare. The case herein presented conforms to the general rule which holds that fetal edema reflects maternal toxicity. The unusual manifestation of the effect of toxicity prompts the presentation of the findings.

Mrs. M. M., housewife, aged thirty-one years, was first seen in the Out-Patient Department of The Lutheran Hospital of Manhattan on May 28, 1936. Her family and personal histories were negative with the exception of an appendectomy in 1931. Several days following the operation she had a spontaneous miscarriage at the fifth month.

When first seen the fundus was the size of a four months' gestation, pelvis negative, general physical condition excellent. Her blood pressure was 150/90. This was called to her attention and she was advised to abstain from proteins and salts; to rest in bed twice daily; to limit fluids and to purge herself every third day. On this regime the blood pressure dropped to 134/84 and the urine, which previously had a trace of albumin, became clear. She was seen at biweekly intervals. On October 8, a marked increase in the size of the fundus was noted. In addition, blood pressure had risen to 150/92 and she complained of vomiting, headache, and blurring of vision. Ophthalmoscopic examination was negative and x-ray of the abdomen failed to reveal any gross pathology in the fetus. She was advised to rest in bed at home.

side of the neck pulsated with each cardiac impulse. The lower lobes of both lungs were compressed and the heart was displaced up into the left axilla. The maximum circumference of the abdomen was $68\frac{1}{4}$ inches. The engorgement of the veins of the abdominal and chest walls was marked. The distention of the abdomen and the edema of the legs are too well shown in Fig. 1 to need further comment.

The blood count showed hemoglobin, 27 per cent; white blood cells, 9,000; reds, 2,040,000. The Wassermann blood chemistry and urine were essentially normal. The blood pressure was 136/86. The temperature was 99.8° F., the pulse 104, and the respiration 28 on admission.

Three immediate indications for treatment seemed obvious: Slow decompression of the cyst, blood transfusion, and forced feeding and forced fluids.

The first paracentesis was done on July 10, 1936, with a very gradual withdrawal of fluid to the extent of 9 gallons, 77 pounds by weight. The second paracentesis



Fig. 1.

was on July 19 and gave $6\frac{1}{4}$ gallons or 54 pounds of fluid. The third paracentesis was on August 14 and amounted to $3\frac{1}{2}$ gallons or 34 pounds, or a grand total of $18\frac{3}{4}$ gallons, 165 pounds of fluid.

Three transfusions of blood by the direct method were done, one each on July 13, 16, and 21. In spite of careful blood typing and cross matching, the third transfusion was followed by an urticarial outbreak and fourteen days of continuous fever which could be explained only on the basis of serum sickness, inasmuch as all physical examination including x-rays of the chest and all laboratory tests failed to disclose any other cause of the fever.

The fever terminated by lysis on August 4, to be replaced as a disturbing factor by an acute serous diarrhea coupled with an acute herpetic glossitis. During this we experienced great difficulty not only in controlling the diarrhea but in feeding the patient and finally had to resort to nasal gavage.

was normal. . . . Pancreas and adrenals were negative. . . . There was no evidence of gross lesions in the kidneys. . . . Ureters and bladder were normal. . . . Uterus and adnexa were normal.''

Microscopic examination of all vital organs revealed no pathology. The fluid possessed all the characteristics of a transudate. Smears were negative save for a few lymphoid cells. Cultures of the fluid failed to produce any growth.

The interpretation of these findings is problematical. We are inclined to the conception that this hydrothorax is an early manifestation of hydrops universalis, although we have no scientific support for this. In the absence of organic pathology other than atelectasis, the etiologic factor must be allocated to the preeclampsia and polyhydramnios of the mother. We have no explanation for this isolated manifestation of toxicity. The case is presented as a rare fetal anomaly; an example of the effects of maternal toxicity on the fetus; an addition to the list of fetal diseases usually found in association with polyhydramnios.

272 WEST 90 STREET
509 WEST 155 STREET

CYCLIC PHENOMENA ASSOCIATED WITH MENSTRUATION, EARLY PREGNANCY AND INDUCED ABORTION IN A HEALTHY WOMAN

CARL G. HARTMAN, PH.D., BALTIMORE, MD., AND RAYMOND SQUIER, M.D.,
NEW YORK, N. Y.

(From the National Committee on Maternal Health, Inc.)

IN HIS recently published book on the *Time of Ovulation in Women*, Hartman¹ emphasizes the element of doubt which still exists on this subject and adds: "I know of only one way of finally dispelling this doubt and that lies with the women themselves. If a sufficient number of intelligent and scientifically inclined women . . . were to keep a punctilious record of their sex life and eventually make the record available for anonymous publication, the cumulative evidence of several thousand such records might help."

As an example of the kind of records wanted the present authors desire to offer the following case history, which includes several points of unusual interest.

The record is that of a young biologist, of nonmedical training, whose menstrual history from 1928 to 1935 has already been published (Hartman, 1936, Fig. 27, page 69). The cycles were mostly over thirty days in length. Early in 1935 she began recording on the calendar two phenomena in addition to the periodic bleeding. These she had noted for some years but had not recorded on the calendar. The first always occurs in the midinterval and consists of an evanescent overabundance of mucous secretion in the vagina, doubtless of cervical origin (Cf. Séguy and Simonnet, 1933).² The second phenomenon consists of turgor and tenderness of the breasts, noticeable only in the last third of the cycle and continuing usually for several days of the menstrual period.

On October 15 her blood pressure rose to 182/104, the trace of albumin reappeared in the urine, and she complained of epigastric distress and headache. The fundus was tense and measured 44 cm. (MacDonald). The fetal heart was audible. Hospitalization was advised.

On October 16 she was admitted to the service. On a Karrell diet, absolute bed rest, sedation and purgation, the blood pressure fell to 150/80 and the urine cleared. She became symptom-free. On October 21 with the blood pressure 150/88, vomiting, headache and blurring of vision recurred. Labor was immediately induced by rupture of the membranes and subsequent small doses of pitocin. The cervix rapidly dilated, but after two hours of full dilatation, vaginal examination revealed a deep transverse arrest and delivery was completed by rotation of the vertex with the Kielland and extraction by Simpson forceps. A female child, weighing 7 pounds 9 ounces and appearing normal in all respects, was delivered. The baby breathed while the cord was clamped and cut, then, with a strong fetal heart palpable, respiration ceased. The infant was transferred to a warm bath and the trachea was aspirated. Alpha lobelin was injected into the umbilical vein and shortly thereafter respiratory efforts were noted and carbon dioxide and oxygen administered. An irregular, gasping respiration resulted and continued for thirty minutes when again respiration ceased. The fetal heart was palpable and stimulation with carbon dioxide and oxygen, alpha lobelin and coramine was continued. The fetal heart became irregular and efforts to stimulate respiration were futile. As it appeared that cessation of the fetal heart function was imminent, a final attempt at stimulation was made by endeavoring to administer an intracardiac injection of adrenalin. The needle was inserted into the thorax through the third left intercostal space, close to the sternum. When the piston of the syringe was drawn up to determine whether or not the heart had been entered, there was drawn up 2 c.c. of a clear, straw-colored fluid. This was ejected into a test tube and more of the same type of fluid obtained. At this time it was noted that the fetal heart had ceased. The needle was then inserted into the right thorax and identical fluid was obtained. Abdominal paracentesis was then performed without result.

The necropsy showed the following relevant findings. "The body is that of a very well-nourished and developed baby, with no apparent congenital anomalies. The head appears somewhat cyanotic. There is a superficial abrasion just below the right eye. There is a moderate degree of edema of both lids. There is no edema of the extremities. . . . On reflecting the scalp there was moderate evidence of caput succedaneum. A window was cut in both sides of the calvarium. There was no evidence of subdural hemorrhage. . . . The cerebral hemispheres were removed and there was no evidence of hemorrhage in the brain substance. A small triangular rent was found just above the level of attachment of the falx to the tentorium. There was no hemorrhage in this area. . . . The pons, cerebellum and medulla were all normal. . . . The chest plate was removed . . . a bilateral hydrothorax was seen. The fluid present was pale amber in color and clear. The right pleural sac contained 100 c.c. of the fluid and the left sac contained 43 c.c. The specific gravity of the fluid was 1.014. . . . The lungs were collapsed toward the hilus. Both were firm in consistency and did not crepitate. Section revealed a typical atelectasis. . . . The pericardium was normal. The heart was normal in size and position. Careful examination failed to reveal congenital anomalies of the heart or great vessels. The myocardium was not remarkable. . . . The thymus weighed 17 gm. . . . On opening the peritoneal cavity an escape of gas was noted, due to the air inadvertently introduced during paracentesis. There was no fluid or exudate present in this cavity. Careful examination failed to reveal abnormality in the gastrointestinal tract. . . . The liver, gallbladder and biliary ducts were negative. . . . The spleen

An intermenstrual bleeding occurred in the succeeding cycle, the mucous secretion from the second succeeding cycle on, breast symptoms not until the fifth succeeding cycle.

This case history offers one more protocol, carefully and intelligently recorded, pointing to midinterval ovulation. It furthermore is an example of the kind of data we should like to acquire in large numbers. Physicians soliciting such records should look first and foremost to the reliability of the person keeping the record and her conscientiousness in putting the data on the calendar at the time and never from memory, days or weeks later.

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PERSISTENT FETAL TACHYCARDIA AND NEONATAL INTESTINAL OBSTRUCTION DUE TO INTERNAL HERNIA BENEATH THE UMBILICAL VEIN

RICHARD B. SCHUTZ, M.D., AND A. M. ZIEGLER, M.D., KANSAS CITY, MO.

THE following case is being reported as a rare type of hernia with obstruction in the newborn, in which the mechanics were such as to partially obstruct the umbilical vein as it passes through the ligamentum teres from umbilicus to liver, and to such a degree that compensatory fetal tachycardia was produced, and finally intestinal obstruction.

The patient was a twenty-seven-year-old primigravida, who was normal physically except for a slight secondary anemia. The Wassermann test was negative. The prenatal course was uneventful except for a moderate polyhydramnios and a persistent edema of the feet and ankles. In spite of excessively hot weather and copious perspiration, the specific gravity of repeated urine specimens remained below 1.005, until just a week before the onset of labor when it became normal.

At five and one-half months the fetal heart sounds were first observed. They were regular and easily heard, but the rate was 160, and on repeated examinations, until term, varied from 160 to 180 per minute.

Two weeks before term, on July 13, 1936, premature rupture of the membranes occurred, followed on the next day by a vigorous labor of three hours' duration, which resulted in the spontaneous delivery, O.L.A., of a female infant weighing 5 pounds and 12 ounces. During labor the uterine contractions were so severe as to require inhalation ether to control them, and the heart sounds, though regular, ranged in rate from 180 to over 200. Though the baby required very little resuscitation the heart rate did not fall below 170 for the first thirty-six hours, postpartum. Within a few hours after birth there began a series of profound cyanotic spells requiring coramine and O₂-CO₂ for relief. Feedings were regurgitated from the first and continued thus, so fluids were given subcutaneously. After twenty-four hours the infant frequently regurgitated brownish and slightly blood-tinged mucus. Urine and several meconium stools were passed. The temperature varied from 97° to

If we are to judge from what occurs in the monkey cervix upon injection of estrone (e.g. Amniotin, Squibb), we may interpret the excess mucus secreted by the cervix in the midinterval as an expression of a high level of the hormone in the blood stream at that time.

The fullness of the breasts, on the other hand, is an expression of the activity of the corpus luteum hormone. This conclusion is in accord with theoretical considerations and is borne out by two observations:

1. The continued and increasing breast turgor during the pregnancy, so long as it continued and sixteen days after abortion.

2. By the nonreappearance of the symptoms for five cycles following the abortion.

This may be due to failure of ovulation or to refractoriness of the previously hypertrophied mammary parenchyma during the two months of pregnancy.

The absence of breast symptoms for several months argues also for the genuineness of the woman's subjective observations and lends confidence to the record, as reflecting physiologic conditions rather than states of mind or realization of expected phenomena.

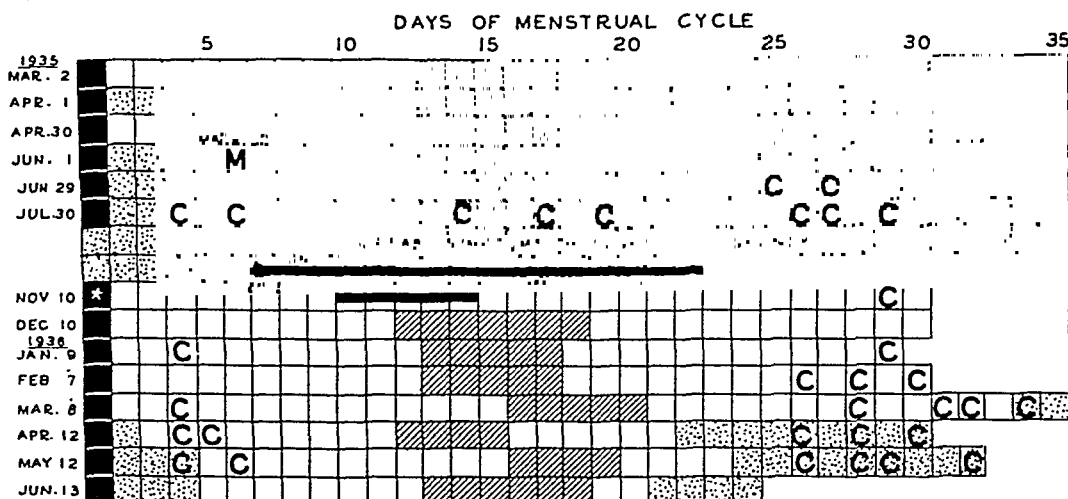


Fig. 1.—Chart showing carefully recorded menstrual history and associated phenomena of a thirty-one-year-old woman, married June 6, 1935 ("M" in chart). On abscissae, days of menstrual cycle. Black squares, first days of the menses (dates given at left). Black square with white asterisk, first menstruation following the induced abortion. Cross-hatched bars, days on which abundant cervical mucus appeared in vagina. Stippled bars, breast symptoms. C, coitus without use of contraceptives (coitus at other times when the vaginal pessary was used is not indicated in chart). Uterus emptied by curettage Oct. 12, 1935 (black dot in chart); horizontal black column thereafter marks uterine bleeding following curettage; breast symptoms continued for the same period, then disappeared for more than five months. Second black bar, light bleeding in the midinterval of succeeding cycle.

In the chart are recorded (C) copulations without the use of contraceptives. The times when a vaginal occlusive pessary was worn were not entered and are not reported. The couple, it may be added, are trying out the "safe period" according to our calculations and, not wishing a family for several years, practice birth control in the ovulation days approximately according to Knaus and Ogino. But during a vacation trip into the mountains in August they were careless, and the wife conceived on one of these days: thirteenth, sixteenth, or eighteenth of the cycle, day thirteen being the most likely. The uterus was curetted by an unknown physician on October twelfth, presumably sixty-one days after conception.

Then uterine bleeding was noted for sixteen days. The first menstruation thereafter began twenty-nine days after the curettage.

4. Probably during labor a larger loop of bowel passed through the aperture and torsion occurred. As the obliterating process progressed in the umbilical vein, it became shorter and more firm, thus increasing the pressure on the bowel and its mesentery, completing the obstruction.

5. The heart rate fell to normal as the infant's O_2 to CO_2 ratio became restored.

6. The striking cardiac irregularity that followed was due to the toxemia attendant on the obstruction and pneumonia.

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201 PLAZA THEATRE BUILDING

THE ELLIOTT TREATMENT AS PROPHYLAXIS FOR GONORRHEA IN THE FEMALE

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(From the Department of Obstetrics and Gynecology, Emory University School of Medicine)

PROPHYLACTIC treatment for gonorrhea in the male has been used for years with gratifying success, but comparable methods are discouragingly inefficient when applied to the female.¹ One has only to consider the principles of chemie prophylaxis and at the same time review the different anatomic and pathologic bases of gonorrhea in the two sexes to appreciate the reason for this. In the male, gonorrhea begins as an inflammation of the terminal portion of the pendulous urethra, lined with resistant stratified squamous epithelium, and almost devoid of glandular structures. In the woman, infective material is deposited upon the urethral meatus and the cervix uteri, both rich in glands and exposed during coitus to a massaging action which tends to implant the gonococcus in deeper layers of tissue than in the man. The anatomy of the female genitals also precludes the self-application of drugs which will remain in contact with the vulnerable surfaces for any length of time.

Noting the prompt response of acute uncomplicated gonorrheal cervicitis, urethritis, and paraurethritis to treatment with the Elliott method (no antiseptics being used), it occurred to me that prolonged intense heat might also be employed to prevent the development of the disease if treatment were begun during the stage of incubation. The number of such cases is small, but the uniform success of the method prompts this report.

CASE 1.—Patient, married, aged twenty-four years, para i, was seen forty-eight hours after exposure to her husband who noted a gonorrheal discharge eight hours

103° F. About thirty-six hours after birth, the heart rate became approximately normal ranging from 140 to 150 and the spells of cyanosis were less frequent. On the third day, however, a persistent irregularity of heartbeat developed with variations in rhythm, rate, and intensity, which was partially relieved for an hour or so after coramine administration. The cyanosis became more severe. A soft upper abdominal distention then appeared which grew progressively worse. Bowel obstruction of some variety was suspected, but fearing to increase the exhaustion of the patient, x-ray studies were omitted and a laparotomy was performed on July 20, although the child's condition appeared hopeless.

Preoperative Diagnosis: Pyloric stenosis, or intestinal obstruction.

Findings.—The obliterating umbilical vein to the liver was elevated 1 to 1½ inches and covered with peritoneum containing an aperture through which protruded a large segment of small bowel. The bowel was not completely obstructed but its position produced a torsion on the mesentery and a pull on the pylorus preventing it from free mobility.

About 10 to 12 cm. of bowel protruded through the aperture in the pseudomesentery from the left to right side and twisted ventrally to the left. The pylorus showed no pathology.

Procedure.—Under local anesthesia a right paramedian incision was made, dividing the layers of the abdominal wall from just below the costal margin to about an inch above the umbilicus. The right rectus muscle was separated and the peritoneum opened. An attempt to elevate the pylorus showed it to be fixed. Further exploration revealed a pseudomesentery over the ligamentum teres through which there was an aperture as described. The ligament was doubly clamped and ligated. This allowed the herniated loop of bowel to return to its normal position and the pylorus to become free. All bleeding points were ligated and the abdominal wound was closed in layers. Tension sutures were placed in the wound. No drainage was employed. Postoperative condition was only fair, and death occurred a few hours later.

An autopsy was performed and there was no evidence of congenital cardiac or pulmonary defect. The final anatomic diagnosis was as follows: Ligated, severed ligamentum teres, mesenteric torsion, patent foramen ovale, acute dilatation of the heart, confluent hemorrhagic bronchopneumonia, uric acid infarcts of the kidney, passive congestion of the liver and spleen, obliterated ductus arteriosus.

A review of the literature on congenital anomalies of the umbilical vein and peritoneum revealed no reports of a similar case. Cullen states that an elevation of the peritoneum over the umbilical vein in the form of a mesentery occurred in three out of fifty cases examined, but there is no mention of an aperture in this structure between the vein and the anterior abdominal wall.

Our hypotheses as to the cause of the clinical phenomena observed in this case are as follows:

1. A knuckle of small intestine entered the aperture between the umbilical vein and abdominal wall not later than five and one-half months of gestation at which time the fetal tachycardia was first observed.

2. The pressure of the bowel against the vein was sufficient to interfere with the passage of a normal volume of oxygenated blood from the placenta to the fetus. In this manner the ratio of CO₂ to O₂ was increased in the fetal circulation.

3. There became necessary a compensatory increase in the fetal heart rate to provide sufficient oxygen to the fetus.

probable that the number of treatments should be proportional to the time elapsed between exposure and the institution of therapy. In that case, a patient seen near the end of the average incubation period of gonorrhea would require about as many treatments as would a case of early uncomplicated gonorrheal urethritis and cervicitis.

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384 PEACHTREE STREET, N. E.

IMPACTED AND INCARCERATED CERVICAL FIBROID COMPLICATING PREGNANCY

SUPRAVAGINAL HYSTERECTOMY

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(From the Obstetric Service of the Polyclinic Hospital)

MRS. A. V., thirty-eight years old, Italian, married fifteen years, one child, thirteen years old. Last menstruation, middle of February.

During April, 1936, the patient complained of uterine bleeding, following two months' amenorrhea and pain in the pelvis. A diagnosis of impacted fibroid complicating pregnancy was made and operation advised. At that time there was a possibility of doing a myomectomy and the patient was so informed. She did not accept the advice and was not seen until six weeks later.

On June 5, patient was admitted to Dr. Ladin's Service at the New York Polyclinic Hospital. She stated that during the week prior to her admission, she suffered from very intense pressing pains in the pelvis and lower abdomen, had difficulty in urination and defecation and was unable to move about. There was no uterine bleeding.

Preoperative Findings.—Bimanual examination on admission revealed that the mass had grown much larger since April and was thoroughly incarcerated in the pelvis. The cervix pointed upward and rested against the symphysis, and palpation of the tumor with the finger in the cervical canal showed that it consisted principally of a submucous fibroid, springing from the posterior wall of the cervix. The uterus and tumor filled the entire pelvis and extended upward to midway between the symphysis and umbilicus, especially on the right side. Complete and satisfactory bimanual examination was impossible because of the impaction of the pelvic tumor, but several fibroids could be palpated through the abdominal wall. The upper left cornu presented some fluctuation, evidently the site of pregnancy. In view of the size, position, and especially because of the submucous type of the cervical fibroid and its impaction, a myomectomy was out of the question and a hysterectomy was decided on.

Operation.—A median incision was made in the lower abdomen. Preoperative findings were confirmed. Notwithstanding the large abdominal incision it was impossible to budge the uterus out of the pelvis by traction until both infundibulopelvic

after coitus. No evidence of disease being found, she was given a series of twelve Elliott treatments. Observation over a period of two years failed to disclose the occurrence of gonorrhea.

CASE 2.—Patient, married, aged thirty years, para i, was exposed to her husband on his return from a trip. He noted a gonorrheal discharge eight hours after the intercourse, and the patient presented herself forty hours after the exposure. No evidence of the disease was found and Elliott treatment was begun. Eight treatments were given, and follow-up for six months failed to show evidence of disease.

CASE 3.—Patient, single, aged twenty-four years, para 0, was exposed on two successive days to a man known to have latent gonorrheal prostatitis and seminal vesiculitis. Examination proving negative, treatment was instituted sixty-four hours after the first exposure. Ten treatments were given and the patient was observed for ten months and no evidence of gonorrhea was found.

CASE 4.—A bride, aged twenty-one, para 0, was exposed on two successive days to her husband, the same contact described in Case 3. By this time his discharge had returned and the patient sought treatment forty-eight hours after her first exposure. Examination being negative for gonorrhea, she was given six treatments. This patient was followed only six weeks, but showed no evidence of disease during that time.

CASE 5.—Patient, married, aged twenty-one years, para 0, was exposed eight hours before her husband noticed his gonorrheal discharge. Showing no evidence of disease, she was given ten Elliott treatments. No evidence of gonorrhea was seen in thirty months, during which time she was observed through a pregnancy.

CASE 6.—Patient, married, aged thirty-two years, para i, was exposed through rupture of condom to her husband who was known to have latent gonorrheal prostatitis. A plain tap water douche was taken eight hours after the exposure. No evidence of disease being found, ten treatments were given, beginning forty hours after exposure. Observation for eight months failed to show evidence of gonorrhea.

COMMENT

None of these women apparently had subclinical gonorrhea at the time of exposure. Unfortunately, complement fixation tests were not done. Four patients were known to have had intercourse over varying periods of time without infecting their partners. In only one instance was any other effort to prevent disease used and that was a plain water douche long after exposure. Natural immunity to the gonococcus does not exist, and it is probable that most of these women would have developed gonorrhea.

The technic of treatment excluded the use of douches, injections, and topical applications. The vaginal bag only was used in this series, but it might add to the efficiency of the method if a urethral applicator were used in series with it. Maximum temperature and pressure were given for forty-five minutes on the third day and for one hour thereafter. No burns were observed, and one patient was treated throughout her menstrual period without ill effect. The number of treatments was intentionally varied, but this series of cases is much too small to arrive at any definite conclusion as to the minimum number required. It is

THE USE OF A RUBBER BAND FOR TYING THE UMBILICAL CORD

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BLEEDING from the umbilical cord of a newborn baby occasionally is difficult to control and is fraught with some danger to the baby as well as being the cause of considerable worry to the doctor and family. The umbilical cord, of course, shrinks somewhat during the early hours of life whereas the material ordinarily used to tie the cord does not contract correspondingly.

A very simple and efficient method consists in wrapping an ordinary small commercial rubber band around the cord. A band an inch and a half long can be wrapped around the cord six or eight times without difficulty. More than one band can be used, of course, if desired. Each strand of the band contracts as the cord shrinks, maintaining constant pressure of a considerable degree.

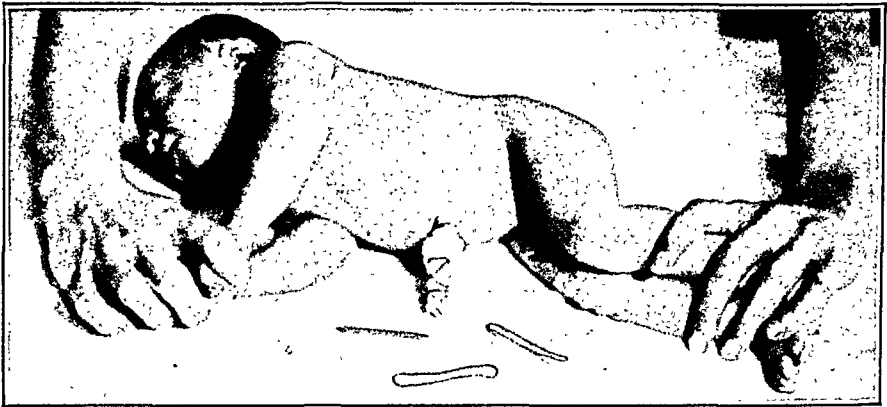


Fig. 1.—Newborn baby, showing dressing on umbilical cord and type of rubber bands used for winding around cord.

We have used this method for the past ten years and found it useful. The method is so simple, it has no doubt been used by others but I have not seen it mentioned. Our usual method of handling the cord has been to tie it with umbilical tape and then, following the late Dr. J. Whitridge Williams' idea of making the after-treatment of the cord as nearly fool proof as possible, we have wrapped a small alcohol gauze sponge about the cord, covering the end of the cord and leaving a little room near the abdominal wall to allow for folding the cord back under the belly band without exerting any pull on the umbilicus. Around this alcohol sponge we have wound the rubber band after the method that small boys once used on their football tubes. Fig. 1 tells the story.

ligaments were ligated and the broad ligaments were divided. It was only then that the uterus was lifted out of the pelvis into the abdominal incision. The right ovary contained the corpus luteum of pregnancy, the left ovary was small and sclerotic, but because of the excessive varicosities of the left broad ligament, it was decided to remove that ovary as well as the right which contained the corpus luteum. A supravaginal hysterectomy with a very low cervical incision was performed together with a bilateral salpingo-oophorectomy. The appendix was not removed. The patient made an uneventful recovery and was discharged seventeen days later.

Histologic Report by Dr. A. S. Price was: The specimen consisted of a large uterus measuring 15 cm. in length, 15 cm. across the fundus. Near the middle portion of the specimen, there was a cervical orifice about $2\frac{1}{2}$ cm. in diameter. Imbedded in one wall of the cervix, and protruding below, was a tumor nodule about 10 cm. in diameter. The uterine cavity was found to be displaced to one side by a

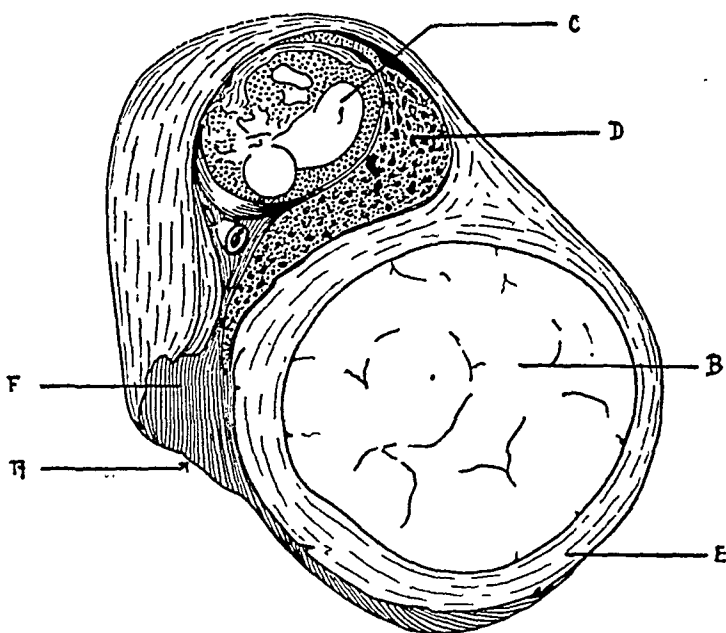


Fig. 1.—Sectioned uterus, showing relation of fibroid to pregnancy. A, External os; B, cervical fibroid; C, fetus; D, placenta; E, cervical wall; and F, cervical canal.

tumor nodule about 7 cm. in diameter found in the fundus. When the specimen was incised, the cervical tumor was hemorrhagic and degenerated. The tumor in the side of the fundus was hard, hyalinized, and showed small areas of necrosis. The fetus was apparently about four and one-half months of age.

Microscopic examination of the uterine muscle showed thinning, yet hypertrophy, of the muscle fibers. To the uterine wall were attached placental and chorionic elements. The endometrium showed a decidual reaction of pregnancy. The uterine tumors showed extensive necrosis, and one showed hemorrhage.

Diagnosis.—Degenerated fibromyomas of cervix and uterus complicated by pregnancy.

This case presents an object lesson as to the question of interference or the expectant plan in the treatment of fibroids complicating pregnancy. In view of the thinning of the wall of the uterus at the site of pregnancy, there is no doubt that the expectant plan of treatment would have resulted sooner or later in the rupture of the uterus.

organization has passed out of existence. I refer to the American Child Health Association which did so much to improve the welfare of infants and children in this country. The parent society is gone but many of its offspring continue, and among them is this organization of ours which is finding a definite field of activity and usefulness.

Since our last meeting the Social Security Act has become a fact and inasmuch as it contains in Title V provision for Maternal and Child Health Services it becomes of vital interest to us.

One of the important functions of our organization is to promote interest and activity in maternal welfare which can be accomplished only by and with that part of the medical profession which is concerned with maternity care. There is no other group of persons who can render this service to the mothers of this country, and both the doctors and laity must realize this fact. The former (physician) must supply the leadership and assume the responsibility; the latter (public) must supply the material, the institutions and the money, either through gifts, fees, insurance, or taxes.

Financial support must be forthcoming. The Federal Government and the States are now cooperating in plans which will assist enormously in this movement, especially so far as administrative organization and education are concerned.

There is still the most important step to be completed and that is the furnishing of services, especially by professional groups of doctors and nurses, so that every mother will receive adequate care during the antepartum, intrapartum and postpartum periods. This means complete maternal care in the home or in institutions, either by the private physician or by organized groups of doctors and nurses and in some sections by midwives.

Two of the fundamental concepts back of the activities of our committee have been that the interested doctors should assume the leadership which is inalienably theirs and that plans should be evolved in local communities which take cognizance of both the needs and resources of those communities. It is fully recognized that both advice or suggestions and financial assistance might be required. On the other hand, it must be realized that no community can permanently carry out successfully a plan for which it does not furnish the leadership and support. Individuals and communities must, in a large measure, ultimately pay in some way or other for the services which they receive or the plan cannot survive indefinitely.

It has been most gratifying to note the progressively increasing interest and activity on the part of physicians in some of the states in promoting maternal welfare. This is shown by the formation of state committees which are working in conjunction with the state medical societies and state boards of health in developing state-wide plans and in stimulating local medical societies to form committees to sponsor the programs for their own communities.

How much our American Committee has had to do with this progress is impossible to state, but it is, at any rate, gratifying to know that the purposes of our organization are gradually being developed as the result of some influences which are leavening the medical profession, the laity and other interested groups.

There have been many factors at work for some time and there have been many obstacles which are slowly being overcome. One of the highest hurdles is jumped when a proper understanding of motives and objectives is reached through the cooperation of the health departments, the medical profession and the laity.

There now seems to be a much better mutual understanding in many of the states than has heretofore existed, and there would seem to be no reason why a similar basis of activity cannot be extended to all of our states. There is no

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

THE AMERICAN COMMITTEE ON MATERNAL WELFARE, INC.

PROCEEDINGS OF MEETING HELD AT KANSAS CITY, MISSOURI,
MAY 13, 1936

Chairman's Address—Dr. Fred L. Adair, Chicago

The Missouri Plan for Maternal Welfare and Child Care—Dr. Ralph R. Wilson,
Kansas City

Maternal Mortality in Georgia During the Year 1935—Dr. Emmet D. Colvin, Atlanta
Abortion and Its Relation to Fetal and Maternal Mortality—Dr. Fred J. Taussig,
St. Louis

Maternal Welfare Under the Social Security Act—Dr. Martha M. Eliot,
Washington, D. C.

The North Dakota Committee on Maternal Welfare—Dr. John H. Moore,
Grand Forks

CHAIRMAN'S ADDRESS

FRED L. ADAIR, M.D., CHICAGO, ILL.

THIS is in reality the second meeting of any size with a more or less formal program which has been held by our American Committee on Maternal Welfare. Those of you who were privileged to attend the last meeting learned something of the objectives of our committee and also heard about the plans which were being put into operation in various parts of the country:

Dr. A. J. Skeel told you of the plan in Cleveland which has worked so successfully there that it has been extending throughout the state and has passed over its borders to be adapted to the needs of other communities.

Dr. A. W. Bingham outlined the Organized Maternal Welfare Work in New Jersey, and this movement has been carried along with increasing momentum.

Dr. J. K. Quigley described the Maternal Welfare Work in New York which is being improved and augmented month by month.

Pennsylvania has moved forward rapidly in carrying out "The Plan of Action, Aims and Progress of the Pennsylvania Commission on Maternal Welfare" as outlined to us by Dr. James S. Taylor.

The interest in and the effect of the meeting in Atlantic City was so encouraging that it seemed very desirable to attempt a similar one in the Midwest at the time of the session of the A. M. A. The meeting today is the sequel at which other plans and ideas will be presented.

Since the last session two more organizations have been added to our list: The American Hospital Association and the National Organization for Public Health Nursing. Unfortunately an older society which was in reality the parent of this

special committee of five members to study the subject and bring in a report for the next annual meeting. The work of this committee has been entirely of the pioneer type; and, by the necessity of the time allotted and the lack of precedent to follow, that committee has borrowed freely from programs of cities, counties, states, national organizations and, in a few instances, foreign countries. I doubt that in the recommendations this committee offered at the state meeting there is a single original idea; it is merely a compilation and organization of efforts and plans used elsewhere.

I might add here that, following the report of the Special Committee on Maternal Welfare at the state meeting in April, 1936, the Association moved that such a committee be continued as a standing committee in the future. At least there appears to be rather favorable setting for such type of permanent work.

PART I

MAKING THE PROFESSION "MATERNAL-WELFARE CONSCIOUS"

I. Summary of Report of Special Committee:

In preparing the program for Part I, the Special Committee for the Study of Maternal Welfare was generously assisted by the State Board of Health. Some of the members of the Board of Health accepted invitations to each of the meetings of the Special Committee and the entire staff of the office of State Health Commissioner held their services open for requests.

A. Specific accomplishments thus far:

1. Changes in the standard birth certificates have been proposed and accepted by the State Board of Health (See appended blanks).

a. Mode of delivery data

b. Assistance to Committee on Crippled Children

2. A questionnaire form has been proposed and accepted by the State Board of Health to be used as the source of supplemental information in all cases of maternal deaths occurring in the state.

3. With the advice and consent of Dr. E. J. Goodwin, editor, a "Query Column" has been established in the *Missouri State Medical Journal* to be edited by members of the Maternal Welfare Committee.

4. A scientific exhibit was prepared and presented at the state meeting this year.

5. This same exhibit was presented to the American Medical Association for display at Kansas City in May, 1936.

6. A Missouri morbidity standard has been established as follows: "A puerperal case shall be considered morbid whose temperature runs a daily peak of 100.4° F. or above for three consecutive days excluding the first twenty-four hours."

7. Speakers on the subjects of various phases of maternal mortality have been furnished the following organizations during the year:

a. The medical section of the Missouri Academy of Science

b. The Missouri Public Health Association

c. The Kansas City Southwest Clinical Society

8. The State Board of Health has been kind enough to furnish the Maternal Welfare Committee a duplicate report of all maternal deaths occurring in the state each month, for purpose of collecting data desired.

9. Each member of the committee has been assigned specific committee work as follows:

a. Scientific exhibits

b. The midwifery problem

c. Criminal abortions

d. Lay publicity

e. Editor for the "Query Column"

f. Legal problems

reason why the state boards of health, cooperating with federal agencies, cannot furnish the necessary administrative machinery, financial assistance and some of the leadership in developing state-wide programs for complete maternity care. The medical profession and nursing organizations must furnish leadership, render service and carry out educational programs for doctors, nurses and the laity.

The state programs for maternal welfare have been, are being, and will be developed, adopted and put into effect by the various states. If interested groups of doctors do not bring the medical profession into the programs, it will fail because no plan not ultimately acceptable to and accepted by them can succeed as there is no other agency which can successfully carry on a comprehensive program of maternal care except those who are trained in the practice of obstetrics. The doctors, nurses, and the laity must work together in safeguarding motherhood to the detriment of none and to the benefit of all.

THE MISSOURI PLAN FOR MATERNAL WELFARE AND CHILD CARE

RALPH RUST WILSON, M.D., KANSAS CITY, MO.

INTRODUCTION

- I. Explanation of name for plan
- II. Conditions one year ago
 - A. Practically virgin soil
 - B. First efforts on part of Missouri State Medical Association to be interested in the field
 - C. Average age of physicians in towns of 10,000 or less is 57.3 years
 - D. State Board of Health
 1. Political appointees and an unstable organization
 2. Divergence of opinions to that of the State Medical Association in the years past
- III. Appointment of Special Committee for study of Maternal Welfare and Child Care, May, 1935
 - A. Constituency:
 1. Five practicing obstetricians
 2. Three practicing orthopedists
 3. President of Missouri State Medical Association, ex officio
 4. Executive-Secretary of Missouri Medical Association, ex officio
 - B. Organization and Problems of the Special Committee
 1. Some plan of making the profession itself "maternal welfare conscious" (See Part I)
 2. Relationship to the State Board of Health with respect to Social Security funds (See Part II)
 3. Promotion of "lay" cooperation and education (See Part III)

In speaking of the title as it appears on our program, I wish distinctly to remove any inference that any of us here in Missouri working in maternal welfare have an original plan or program that is worthy of being copyrighted under such a name. As you well know, there was no especial interest in maternal welfare in Missouri until consideration of the Social Security Bill was brought before the American people, except for some interrupted work started by the American Legion. With that as a stimulus the Missouri State Medical Association in May, 1935, appointed a

PART II

RELATION TO STATE BOARD OF HEALTH WITH RESPECT
TO SOCIAL SECURITY FUNDS

I. Advisory Committee for the State Board of Health

A. Advisory Committee Personnel:

1. President of State Medical Association
2. President of State Dental Association
3. Representative of State Nurses Association
4. Representative of School of Medicine, Missouri University
5. Representative of School of Medicine, Washington University
6. Representative of School of Medicine, St. Louis University
7. Representative of State Tuberculosis Association
8. Representative of State Public Health Association
9. Representative of Missouri Association of Social Welfare
10. Representative of American Society of Pediatrics
11. Chairman of Maternal Welfare, State Medical Association

B. Duties of Advisory Committee:

1. Quarterly meetings with expenses paid
2. Aid in programs
3. Aid in future problems

II. Program for the State of Missouri Under the Social Security Plan

A. Objectives:

1. To benefit mothers and children in Missouri
2. To benefit physicians in Missouri
3. To promote lay education and principles of preventive medicine (all could have been directed to this end perhaps)

B. Agencies and Method of Administration:

1. Dispensation of Funds "A" and "B"
 - a. By Missouri law such funds dispensed only through Department of Education
 - b. Personnel responsible only to Division of Child Hygiene

C. Personnel of Staff:

1. Medical Director of the Division of Child Hygiene
2. Assistant Director of the Division of Child Hygiene
3. One full-time obstetrician (field worker)
4. One full-time pediatrician (field worker)
5. One full-time Public Health Director (field worker)
6. Three nurses with public health training
7. Auxiliary speakers to assist field workers

D. Field Program

1. Division of State into Working Units of:

- a. Councilor districts for purposes of:
 1. Future appointments
 2. Supervision of own work
- b. Local medical units, except urban territory

10. With the idea of establishing an annual custom, arrangements were made for a Maternal Welfare Committee Dinner at the state meeting. At this meeting members of the committee presented interesting cases of maternal deaths occurring in their own practice. Members of the Association who were known to have been so unfortunate as to have had maternal deaths were invited to sit in for this report and the subsequent comments.

11. By the consent and cooperation of the Program Committee and the officers of the State Association, a nationally known obstetrician, Dr. Joseph L. Baer, Chicago, was invited to give a critique of the presentations of the cases made at this dinner. All members of the Association, however, were welcome at both the dinner and the discussion thereafter by purchasing a ticket.

12. On the following morning Dr. Joseph L. Baer appeared as a guest speaker before the General Assembly, under the special auspices of the Committee on Maternal Welfare.

13. The membership of the Missouri State Medical Association has been surveyed and men throughout the state with special obstetric training or experience are classified in a reserve position to be used as auxiliary forces in carrying out special ideas or schedules.

B. Proposed objectives:

1. That the above program, as outlined, should be fostered and carried out so far as advisable and feasible for the next three years.

2. That the state be divided into territorial units; e.g., the Councilor Districts, for the purpose of unified investigations and approaches.

3. That the President of the Association appoint a special assistant from the respective Councilor Districts who is interested in obstetric problems in order to further any program or schedule.

4. That the Committee on Postgraduate Work assist the Committee on Maternal Welfare in establishing "refresher courses" and in doing extension work over the state.

5. That the Committee on Scientific Work assist the Maternal Welfare Committee in selecting one nationally recognized speaker for each Annual Meeting of the Association.

6. That there shall be the establishment of an annual award, although nominal in monetary value, for the best article appearing in the *Missouri State Journal* along the lines of maternal mortality during the year.

7. That some influence be established and popularized to promote the universal application of the Wassermann test on all expectant mothers.

8. That hospitals or institutions receiving referred cases from outlying districts be encouraged to separate maternal morbidity and mortality in those so-called "mussed-up" cases from those entering by regular routine.

9. That the Woman's Auxiliary of the State Association be approached and an attempt made to interest them in the activities of the Committee on Maternal Welfare.

10. That the Maternal Welfare Committee hold itself in constant readiness to provide State and Federal agencies with technical advice.

11. That the Committee cooperate so far as feasible and advisable with the American Committee on Maternal Welfare, Inc., in order to emphasize the significance of maternal mortality.

12. Assist Children's Bureau in the special study of stillbirths.

8. The staff members employed in the Division of Child Hygiene shall pay their entire travel and expenses from the amount allowed each individual for travel or expenses, and must in addition furnish any instruments or materials necessary in their work and not otherwise furnished by the State Board of Health.

9. The library of the State Board of Health is open to each staff member but any periodicals or books purchased by staff members shall be at their expense and will not be paid for from funds of the State Board of Health, unless so directed by the State Commissioner of Health.

10. Harmony among staff members is essential and petty bickering or personal gossip will not be tolerated. While in the field, whether during business hours or at other times, the employee is to remember that he is a representative of the State Board of Health and shall at all times so conduct himself. The State Board of Health will be largely judged by the type of personnel employed. The success of the administration of the Health Department will reflect credit upon the staff members and vice versa.

11. Comments or criticism heard in the field should be reported to the Division head who in turn will report such comment to the State Commissioner of Health.

12. Correspondence from staff members to the central office shall be addressed to Dr. E. T. McGaugh, Attention, Division of Child Hygiene.

PART III

RELATIONSHIP TO "LAY PUBLICITY" AND GENERAL PUBLIC EDUCATION

I. Responsibilities and Cooperative Duties of Missouri State Medical Association. (Incomplete to date.)

II. Responsibilities and Cooperative Duties of Missouri State Board of Health. (Incomplete to date.)

III. Responsibilities, etc., of Public Health Service. (Incomplete to date.)

IV. Responsibilities and Cooperative Duties of the Missouri Department of Education. (Incomplete to date.)

V. Reciprocation with Recognized Lay Health Organizations. (Incomplete to date.)

VI. Cooperation with Department of Extension Work of the University of Missouri. (Incomplete to date.)

SUMMARY

I. At the end of a year's work the Special Committee of the Missouri State Medical Association for Maternal Welfare has been made a permanent committee of five whose terms of office shall be three years—so staggered as to have two members retire each year to give place for two new members yearly.

II. The Missouri Plan of administering the Maternal Welfare funds has been accepted by the Children's Bureau.

III. Funds have already been received for the first year's work.

IV. The field workers are now spending a period of observation in preparation for active work to begin July 15, 1936.

V. A friendly relationship has finally come to exist between the Missouri State Medical Association and the Missouri State Board of Health.

VI. As yet, the plan can be submitted only in the form of a synopsis as the context will be derived from experiences encountered in its application. Thus, perhaps, before a final text is completed, it will have undergone many alterations.

VII. The State of Missouri has accepted the challenge of the high maternal mortality rates existing within her borders.

E. Specific Programs for Field Workers

1. Outline of subjects for Field Workers in Obstetrics:

- a. The mechanism and management of normal labor
- b. The toxemias of pregnancy
- c. The usual complications of pregnancy, with special reference to pneumonia and intercurrent infections
- d. Syphilis and pregnancy
- e. The management of normal pregnancy
- f. The minor ailments of pregnancy and prenatal care
- g. Abortion, miscarriage and premature labor
- h. Hemorrhage, both antepartum and postpartum
- i. Pelvic measurements
- j. The value of a complete physical examination early in pregnancy
- k. Breech presentation and the method of its management, with special reference to its early diagnosis in labor
- l. Forceps, versions and episiotomies
- m. The management of occipitoposterior positions
- n. Puerperal sepsis with special reference to contaminations by the attendants as well as exacerbations of patient's own infection
- o. Cesarean section with special reference to the obstetric indication as well as the surgical facilities at hand
- p. Contraception and sterilization with special reference to legal aspects, as well as medical technic.
- q. Significant laboratory procedures in obstetrics
- r. Hemorrhage and discharge in the nonpregnant

2. Outline for Field Workers in Pediatrics

3. Outline for Field Workers in Public Health Nursing

4. Outline for Field Workers in Dentistry

5. Outline for Auxiliary Field Workers

- a. Duties of this group are largely one of educational lectures according to specific needs
- b. Salaries are to be on "piece-work" basis

F. Rules governing Members of the Staff:

1. The Division of Child Hygiene does not practice medicine.
2. The staff members of the Division of Child Hygiene shall not enter into any argument concerning politics, administration of the State Board of Health, or policies of the State Board of Health. They shall, however, become familiar enough with the regulations of the State Board of Health that they shall be able to discuss intelligently questions pertaining to programs or policies.
3. Physician members employed by the State Board of Health must not only be reputable physicians with high professional qualifications but shall be members of the County, State and American Medical Association. They shall further become members of the State Public Health Association and the American Public Health Associations.
4. All members of the nursing staff shall be members of the State Nurses Association, and the National Organization for Public Health Nursing.
5. Each physician and nurse employed by the State Board must be licensed to practice medicine or nursing in the State of Missouri.
6. No member of the Staff shall obligate the State Commissioner of Health or any department head in any manner without first consulting the individual concerned.
7. In no case shall they directly or indirectly obligate the State Board of Health financially.

number of deaths were due to eclampsia. Seventy-three per cent of the women dying of eclampsia were not attended by a physician prior to the onset of convulsions. Twenty-three, or 19 per cent, of the eclamptic patients died undelivered. Forty-five per cent delivered spontaneously and 34 per cent were delivered by operative procedures. It was found that the onset of labor was spontaneous in 62.9 per cent of the women dying of this condition. Fifty-five per cent of them died without the benefit of hospitalization.

Hemorrhage, including placenta previa, abruptio placentae, and postpartum bleeding claimed 14.9 per cent of the mortalities. The accidents of labor accounted for 2.6 per cent. Hyperemesis, ectopic gestation, and diseases incidental to pregnancy make up a small percentage of the total fatalities in the study.

DISTRIBUTION OF DEATHS AMONG WHITES AND NEGROES

One hundred and eighty-eight, or 52.8 per cent, of 356 deaths were among white women. Evidently the presence of a large negro population in the state is not the factor responsible for our increased maternal mortality rate, as we have so often thought.

Deaths following abortion were higher among colored than among white women. The percentage of deaths due to hemorrhage was twice as high among whites as among negroes. Deaths due to sepsis, eclampsia, and other causes were approximately equally divided between the two races.

The incidence of illegitimate pregnancies was 3.5 per cent among whites and 11.5 per cent among negroes.

PRENATAL CARE

After excluding those women who died from ectopic pregnancies and abortions, there remained 294 who might have received prenatal care, but 68.3 per cent of them died without the benefit of prenatal supervision. Seventeen per cent were credited with having received adequate care, and 14 per cent of them had inadequate or poor care.

PARITY

Primigravidas made up 173, or 48.6 per cent, of the mortalities. The percentage of deaths due to abortions, ectopics, and hemorrhages was more than twice as great among multiparous women. Deaths due to septicemia were 9 per cent higher among the multiparas. Albuminuria and eclampsia caused 52.5 per cent of the mortalities among the primigravidas.

PERIOD OF GESTATION

Two hundred and eighty-two, or 76 per cent, of the fatalities occurred in women who had reached the third trimester of pregnancy. Death occurred during pregnancy in 8.4 per cent; during labor in 4.8 per cent; and 86.8 per cent died during the puerperium.

OPERATIVE DELIVERIES

These are factors of great importance in the etiology of present-day obstetric mortality. Of the 282 women who died in the third trimester of pregnancy, 34 per cent had had some form of operative procedure directed toward delivery. Twenty-five deaths occurred after cesarean sections had been performed; 44 women died following forceps delivery; 29 died after delivery by version and immediate breech extraction; and 5 deaths followed breech extractions. It was found that 32.5 per cent of the patients with albuminuria and eclampsia were delivered by operative procedures.

MATERNAL MORTALITY IN GEORGIA DURING THE YEAR 1935

E. D. COLVIN, M.D., ATLANTA, GA.

DURING the past two years it has been my privilege and pleasure to serve as the chairman of a committee of twenty-one members appointed to study maternal mortality in the state of Georgia, and the following paper is made up of statistics from the committee's annual report to the House of Delegates of the Medical Association of our state.

A form similar to the ones used in the New York, Philadelphia, and the Fifteen States Survey was used in collecting the statistical data. Slight modifications of the questionnaire were made in order to meet conditions existing in our state.

On the tenth day of each month the Bureau of Vital Statistics supplied the committee with a copy of the maternal death certificates filed with it during the preceding month. Identifying information was copied from the certificates onto the questionnaires and these, accompanied by self-addressed and stampel envelopes in which they were to be returned, were immediately mailed to the attending physicians or midwives. If the attendant did not reply after several forms had been sent to him, one of the local district members of the committee then was requested to interview him. Thus, the committee was able to obtain its information before the details of the case had escaped the memory of the attendant.

It is not desired to overburden you with statistics, but a presentation of the following general information will give a rather definite idea of the relative importance of some of the factors which contribute to, and influence maternal mortality in our state.

During the year 1935, 60,424 live births were reported. Of these, 35,634 were whites and 24,790 were negroes. Physicians attended 35,701, and midwives attended 24,482 of these births. Of the 35,701 whites, 30,322 were attended by physicians and 5,201 by midwives. Of the 24,790 negro births, 5,379 were attended by physicians and 19,281 by midwives. A total of 3,968 stillbirths occurred during this same period. Of these, 1,524 were whites and 2,444 were negroes.

Sixty-seven per cent of the reported live births in the state occurred in rural districts. Midwives attended 39 per cent of the live births in the state. Physicians attended 81 per cent of the urban, but only 52 per cent of the rural deliveries.

The maternal death rate for the state during 1935 was 7.1 per cent per 1,000 live births. The infant mortality was 69 per 1,000 live births. Four hundred and thirty-eight maternal deaths occurred during the year, and the committee obtained answers to its questionnaires regarding 356 or 81.3 per cent of these mortalities.

CAUSES OF DEATH

Abortion was the cause of 53, or 14.9 per cent, of the fatalities. Seventy-nine per cent of these deaths were attributed to sepsis and constitute 38 per cent of the total number of deaths due to puerperal infection. Puerperal septicemia was the cause of 93, or 26.1 per cent, of the mortalities. Septic deaths following abortions will increase this figure to 41 per cent and place septicemia as the most frequent cause of death.

One hundred and twenty-three, or 34.5 per cent, of the mortalities were due to the toxemias of pregnancy. One hundred and sixteen, or 32.6 per cent, of the total

Much blame can be placed upon the public for its failure to apply for and cooperate in prenatal care. Over two-thirds of our deaths occurred among women who had not been attended by a physician before he was called to treat the pathologic conditions which claimed their lives. The profession must be willing to instruct and guide the public by continually and persistently giving advice in all matters pertaining to pregnancy. This advice would be especially valuable in controlling deaths due to abortions and toxemia.

The profession alone, without the cooperation of the laity, can make very little progress in decreasing maternal mortality in our state. The public must be advised and it must be strongly urged to cooperate in this problem of such vital interest to it. If it is possible to reduce the number of deaths due to abortions and improperly handled toxic conditions, the death rate for the state will be greatly reduced.

Economic conditions have caused the bulk of rural maternity work to be thrust into the hands of the midwife. It is the duty of the medical profession to demand that the type of her training and the quality of her work be improved. Also, adequate supervision of her work is of paramount importance.

The medical profession of the state cannot undertake to change the economic system, nor are they in a position to bring about a change in the general level of intelligence throughout the state. Ignorance, superstitions, and illiteracy continue to handicap scientific efforts. However, in the interest of the advancement of preventive medicine it is the duty of the profession to undertake to eliminate those factors not of a medical character which increase maternal mortality. Once the cooperation of the public is obtained and a system of maternity service instituted, the death rate from eclampsia alone should be reduced 50 per cent. It is alarming to learn that this almost preventable disease was the cause of 30 per cent of the maternal deaths in the state of Georgia last year.

1040 PONCE DE LEON AVENUE, N. E.

The increasing use of various anesthetic agents which so often interfere with physiologic labor and necessitate a greater operative interference is a rather constant contributory factor in the cause of increased maternal mortality. But anesthesia was a small factor in the causation of maternal mortality in our state during the year covered in this survey. Of the 282 women delivered during the third trimester of pregnancy, 41 per cent did not receive any form of anesthesia. Chloroform was the anesthetic of choice among rural practitioners. Three women died as a result of spinal anesthesia before the contemplated cesarean sections could be started.

METHOD OF ONSET OF LABOR

The onset of labor was spontaneous in 255, or 89.9 per cent, of the women who were in labor during the third trimester of pregnancy. The catheter method was the one most often employed in the induction of labor. Of the patients who were suffering from toxemia, 62.9 per cent developed convulsions prior to or after labor had started spontaneously.

PLACE OF DELIVERY AND PLACE OF DEATH

Only 45.8 per cent of the women who died had had the advantage of hospitalization. Of these, 39.1 per cent were rushed in as emergencies or were in a moribund condition at the time of admission.

INFANTS

From the 282 women reaching a stage of fetal viability, 187 infants were delivered alive. Seven sets of twins and one set of triplets are included in the series.

ATTENDANT AT DELIVERY

Midwives alone attended 19.3 per cent of the fatalities, and in 25.3 per cent they were relieved by physicians after complications had developed. Therefore, midwives contacted 44.6 per cent of the mortalities. Physicians alone were credited with having attended 50.5 per cent of the deaths. During the year covered in this survey, midwives attended 24,482, or 40.5 per cent, of the live births reported in the state of Georgia.

In conclusion, after reviewing the records of 356 maternal deaths, we cannot deny that our maternal mortality should be greatly reduced. It is an outstanding fact that there is a need in rural communities for prenatal care and supervision during delivery—a service which does not exist at this time. It is a mutual problem of the laity and the medical profession. Until organized medicine appreciates the importance of maternal mortality, and until we realize its cause, it is of little use to appeal to the public for its cooperation. Too often we, as physicians, are unwilling to accept the blame for a large number of maternal deaths which studies have shown to be preventable or controllable. An example of this is illustrated by the frequency of failure on the part of physicians to appreciate the signs, delay in reaching a diagnosis, and postponement of definite measures in terminating pregnancy among patients suffering from fulminating toxemias. In this study, many cases were presented in which a preeclampsia, treated expectantly, was permitted to develop into eclampsia. In contrast to these, there are a number of physicians who practice radical procedures and continue to treat extremely ill toxic patients by operative procedures, illustrated by emergency cesarean sections on women suffering from eclampsia.

Too often there is a lack of understanding of just what is meant by prenatal care. To be able to render prenatal care, a physician must not only understand it, but he must be willing to render it conscientiously.

tration area of the United States or about 3,000 for the entire country. The splendid study of New York maternal mortality made under the auspices of the New York Academy of Medicine with check-up of all cases by personal interview and hospital records showed that in 56 out of 357 maternal deaths from abortion no mention of abortion was found on the death certificate. There was thus an error of one in every six death certificates. Let us keep clearly in mind that these were all recorded as pregnancy deaths but not as abortion deaths. If we apply this addition of one-sixth to the total of about 3,000 registered abortion deaths, we get 3,500 as the approximate number that can be included under this head.

And now to come to the search for abortion deaths classified under other heads: In the monograph on abortions* I call attention to an interesting suggestion made by Freudenberg in studying abortion mortality in Prussia. He found that the figures for abortion deaths by some writers almost equalled the total deaths for all women of fertility age. As a check-up on these wild statements he made a comparison of the causes of death in men and in women in the fertile period between fifteen and forty-five years. Where there was an evident discrepancy in favor of the women, as under the head of lung, cardiac and genitourinary diseases, one-half of the total was roughly estimated to be due to concealed abortion deaths. In this way the number of abortion deaths registered under puerperal causes was found to be about one-half of the total. I have attempted a similar comparison between male and female deaths from the U. S. Census reports for 1930, 1931, and 1932, occurring during the period of fertility (fifteen to forty-five years), and the estimated ratio of concealed abortion deaths tallies closely with the figures obtained by Freudenberg.

Under some heads, such as tumors, malformations or certain infectious diseases, the likelihood of misstatement is remote. In other groups there was no apparent discrepancy from the average of 10 male to 8 female deaths. Striking differences were, however, found under the head of:

List No. 129: Peritonitis, cause not specified (1930-32): male 549; female 1004; an average surplus of 152 women per year.

List No. 125a: Yellow atrophy of the liver (1930-32): male 189; female 482; an average surplus of 98 women per year.

In the larger groups we also found a discrepancy under the head of:

List No. 23: Tuberculosis, respiratory system (1930-32); average discrepancy of 3,035.

Group VII. Diseases of the circulatory system (1930-32); average discrepancy of 2,064.

List Nos. 130-131: Acute and chronic nephritis (1930-32); average discrepancy of 1,774.

The total discrepancy from these three causes of death was 6,873. If we assume that one-half of this discrepancy might be due to concealed abortion deaths we would have 3,437 additional deaths.

If now we add all these concealed deaths to the 3,500 previously referred to under the head of pregnancy, we find that the approximate corrected annual deaths from abortion in the continental United States amount to 7,187. Even supposing that we had failed to include a few abortion deaths concealed here and there under other heads, it is inconceivable to me that the total number could greatly surpass 8,000 annually. This would seem a maximum figure.

The average death rate from abortion taken from large hospital and dispensary figures here and abroad is 1.2 per hundred. The sources of this estimate are given in a previous publication. With improved technic of physicians and abortionists,

**Abortion, Spontaneous and Induced, Medical and Social Aspects*, St. Louis, 1936, The C. V. Mosby Co.

ABORTION AND ITS RELATION TO FETAL AND MATERNAL MORTALITY

FRED J. TAUSSIG, M.D., ST. LOUIS, MO.

ABORTION is, I believe, the greatest single factor in fetal and maternal mortality. This is evidenced by the fact that approximately one out of every four or five conceptions terminates in fetal death through abortion and that two out of every five maternal deaths can be ascribed to an abortion. From the available data, in spite of uncertainties, I am convinced that this statement is not far from the truth.

Let me explain briefly how I have arrived at these figures. There is a difference between a guess and a careful estimation. You have doubtless all had occasion at some time to guess at the number of beans in a gallon jar. If, however, you have taken the problem seriously and carefully measured the jar capacity and the size of the bean, the answer should closely approximate the actual number. The same principles apply in the calculation of total abortion deaths. If, in addition, we seek independently the abortion death rate and find that the estimated number of abortions times the estimated death rate tallies approximately with the estimated abortion deaths, I think you will agree that we are near the actual figures. And I think it is of considerable importance for us to visualize this approximate truth instead of assuming an agnostic attitude as some do, or accepting the wild exaggerations that are so frequently made by propagandists.

First as to the number of abortions: Hospital and dispensary figures quite evidently record but a small proportion of the total abortions since so large a number are done secretly without record of any kind. While anxious to conceal the fact of an abortion at the time it occurs, it is the general experience of physicians that women are surprisingly frank in giving information concerning past abortions. From such statements the ratio of abortions to confinements can be estimated. From Dr. Kopp's study of records in New York maternal health centers, there were found to be 11,172 abortions to 27,813 confinements, a ratio of 1 to 2.5. This corresponds to smaller statistics obtained from other urban sources. In the rural districts this abortion-confinement ratio from the figures collected by Plass approximates more closely 1 abortion to 5 confinements. Dividing the 2,400,000 annual births according to the U. S. Census estimate of 42 per cent urban and 58 per cent rural, we arrive at the figure of 681,000 abortions annually in the United States. Let us call this 700,000 abortions, add to this 100,000 stillbirths (figured at 4.2 per cent of the live births) and then the 2,400,000 live births, we arrive at a total of 3,200,000 conceptions of which 700,000 terminate in abortion, or approximately one in four or five conceptions.

Equally troublesome is the estimation of maternal deaths from abortion. The recorded abortion deaths as given in the Census reports are certainly incomplete, since there is ample evidence that a very large proportion of abortion deaths are intentionally concealed for fear of exposure or possible legal entanglements. On the other hand, let it be clearly understood that practically without exception *every death is somewhere on record* in our mortality statistics, even though a different diagnosis may be put on the death certificate. The problem is to find under what head these additional abortion deaths might be concealed. The actual correctly recorded abortion deaths for the years 1930 to 1932 averaged 2,740 for the regis-

trained, physician. Perforation of the uterus is another unfortunate accident only too common under such conditions. With but few exceptions we must advise a "hands-off" policy in the presence of acute infection.

While we are here concerned primarily with problems of mortality, we should not leave out of consideration the very serious and widespread morbidity resulting from this scourge of abortion. It was a realization of these sequelae that largely induced the Russian government to restrict its policy of legalized abortion. Such women are likely to develop in subsequent pregnancies serious complications such as ectopic gestation, adherent placenta, and difficult labors. In other ways their general health and constitution may be undermined by repeated abortions.

If I have been pessimistic in thus presenting to you the wastage of maternal life and health through the widespread prevalence of this practice of abortion, let me add that I am rather optimistic as to the future. This is based upon the following changes that have recently become manifest:

1. A franker facing of the problem of abortion in medical and sociological writings.

2. Better understanding of the causes of spontaneous abortion and its prevention.

3. The awakening of social consciousness, especially in regard to maternal welfare among the poor.

4. Gradual elimination of the untrained midwife.

5. Widespread information concerning birth control and better methods of preventing conception where pregnancy is not desired or is contraindicated.

6. Better training by physicians in the handling of abortion cases. These changes have, however, only just begun. We must do all in our power to hasten their development.

with a decrease in the number done by midwives and patients themselves, this rate is probably a little too high. At any rate we see that the number of estimated abortions (700,000) times the death rate comes very close to the estimated total of abortion deaths (7,187).

Turning now to a comparison of abortion deaths with those following childbirth, we find that the number of registered deaths following pregnancy, childbirth and the puerperal state for the years 1930 to 1932 averaged 14,156. If we deduct from this number the 3,500 abortion deaths registered under this head and about 600 due to ectopic pregnancy, we have approximately 10,000 deaths at confinement compared with about 7,000 abortion deaths, a ratio of 3 deaths from childbirth to 2 deaths from abortion.

So much for the numerical evaluation of abortion as a factor in fetal and maternal mortality. Now a word as to what can be done to prevent this enormous waste of human life: Practically we cannot weigh in the same balance the life of a two-month embryo and the fully developed life of the young mother. Nevertheless the loss of these embryos occurring by the thousands is a serious handicap to the work of the world. It interrupts the important obligations of the mother to her family, it is a serious financial burden, and often leads to partial or even complete disability of the women who have aborted. Nowhere is the ounce of prevention more clearly needed, and this ounce of prevention means the prevention of the undesired or undesirable pregnancy. More widespread information concerning birth control, and better and simpler methods of preventing conception are indispensable to accomplish this end. This would, of course, apply only to the induced and therapeutic abortions comprising together about 70 per cent of the total. Concerning the prevention of spontaneous abortion (the remaining 30 per cent) much has been written and, especially with our increasing knowledge of endocrine pathology, methods of treatment have shown considerable improvement. Physicians either through carelessness or ignorance are frequently remiss in their efforts to hinder a spontaneous abortion. A fuller appreciation of the underlying causes tending to faulty development or premature expulsion of the fetus would result in a definite lowering of the abortion rate. Fetal deaths due to syphilis in the middle trimester of pregnancy could, under proper supervision, be reduced to a very small number. Indeed there is more hope of accomplishment in the prevention of spontaneous abortion than in the larger group of induced abortions in which the physician must cope with a change in underlying social conditions and economic distress.

Coming now to the seven to eight thousand maternal deaths, we must realize that the underlying cause in the larger group of induced abortions is that the illegal operation is usually done under conditions predisposing to infection by a person untrained in surgical technic. The Russian legalization of abortion, quite regardless of how it may have stimulated an increase in the actual number of abortions, has demonstrated that the abortion mortality can be reduced from about 1 per cent to almost one hundredth of that amount by rigidly restricting its performance to qualified physicians working under hospital conditions. Whether a broadening of the indications for abortion is a step in the right direction is worthy of careful consideration. Such a change should primarily be concerned with the relief of the depleted pluriparous mothers of the poor.

Of more immediate concern to the physician is the proper handling of the infected abortions, whether spontaneous or induced. The analysis of maternal mortality made through the Children's Bureau has shown the large part played by the curette in the spread of these infections. Only too often an infection introduced by the instruments of the patient, midwife, or abortionist into the uterine cavity, is carried into the blood stream by the operative zeal of the well-meaning, but poorly

outset. If those three objectives can be attained, we feel that much will have been accomplished in the campaign for better obstetrics.

I would call your attention to the fact that North Dakota is one of 17 states in the Union requiring an internship before a license to practice is issued by the State Board of Medical Examiners and that this rule has been in effect since 1918. It is thus evident that our physicians have had rather better than the average medical training. Our state has, predominantly, a rural population and everyone knows the difficulties surrounding the man with a large rural practice dependent upon him when he attempts to find time for postgraduate instruction. In most instances, finances and the demands of his practice will not permit it.

We feel that if postgraduate instruction is to be made available to our physicians, it must be brought to them. To this end, preliminary arrangements are now under way to hold at least 3 or 4 two-day obstetric seminars during the year. The plan is to have this seminar conducted by some prominent obstetrician from out of the state. We have arranged with 3 District Medical Societies to sponsor such seminars and hold their regular evening meeting on the closing night of the sessions at which time the visiting clinician will be asked to address the society and its guests. The chief subjects to be discussed in this seminar are: (1) Prenatal care, (2) the prevention of infection, (3) the prevention and control of the toxemias of pregnancy, (4) the prevention and management of abortions, and (5) breast feeding. Members of our committee will be ready to assist in the clinics and discussions if requested to do so by the host society, but we are again placing the emphasis where we think it belongs—on the district society.

This will be a very modest beginning in the matter of postgraduate instruction, but we feel confident that the success of our first seminar will create a demand for similar seminars or "refresher" courses on a larger scale and that eventually they will be in demand throughout the state.

I cannot leave the subject of professional education without acknowledging with gratitude the splendid cooperation our committee is receiving from Dr. Maysil M. Williams, State Health Officer for North Dakota. Through her department, sterile obstetric packages are to be made available to private physicians requesting them for home deliveries. With the endorsement of the committee and under the direction of Dr. Williams, a Maternity Nursing Service is to be instituted in one county in the state for a period of one year. We will watch with great interest the work of this Nursing Service.

The committee has stressed the importance of well-equipped, separate obstetric departments in hospitals admitting maternity patients, adequate nursery facilities, and the importance of the isolation of any infected patients. Our hospitals in the larger centers have an excellent rating in these vital points. We have somewhat of a problem in some of the small so-called "maternity homes." These are often nothing more than private dwellings, admitting two or three women for care during labor and the puerperium. The State Board of Administration which licenses all hospitals and maternity homes in the state will be asked to check all so-called "maternity homes," especially in regard to equipment and whether or not registered nurses are in charge.

We entered the field of lay education via radio. The committee prepared a series of eight radio talks, each fifteen minutes in length, and they were broadcast weekly under the name of the North Dakota Committee on Maternal Welfare by Dr. H. E. French, Dean of the Medical School of the University of North Dakota and Chairman of the Committee on Medical Education of the North Dakota State Medical Association. The committee desires to express its thanks to Dr. French for his cooperation in making these broadcasts possible. Subjects presented were: "Prenatal Care," "The Hygiene of Pregnancy," "Diet and Exercise in Preg-

THE NORTH DAKOTA COMMITTEE ON MATERNAL WELFARE

JOHN H. MOORE, M.D., F.A.C.S., CHAIRMAN, GRAND FORKS, N. D.

THE North Dakota Committee on Maternal Welfare is very young. Time will give it maturity without, I hope, diminishing its enthusiasm. It was conceived by the American Committee on Maternal Welfare, Inc., and born by the North Dakota State Medical Association. We trust that neither parent will have occasion to disown its offspring.

We were appointed as one of the regular committees of the North Dakota State Medical Association in November, 1935. Our first major objective was the sponsoring of as many obstetric meetings before the component District Medical Societies of the State as time would allow. Every committee member was assigned a topic and everyone accepted his subject and went to work. The purpose was not merely to present obstetric programs in a hit-or-miss manner but to present a symposium on obstetrics, dealing with the major causes of obstetric deaths. Infections, toxemias, and hemorrhage are the major causes of maternal deaths in North Dakota, just as they are elsewhere.

One of our committee took as his subject, "Maternal Mortality in North Dakota." With access to the files of the Bureau of Vital Statistics, he was able to present the figures for our own state in a convincing manner. I would not have you believe, from this, that North Dakota has a high maternal mortality. On the contrary, it ranks with the best in the country, but our neighbor, Minnesota, with the best record in the nation, has given us a tangible goal to reach, and we are out to equal or better her record!

Emphasizing the importance of the Maternal Mortality Triad, we usually present three papers at each district meeting. Discussion is based on the papers as a symposium after the formal presentation of all of them. We have found that this is by far the best way to provoke discussion. Informal case reports, based on one of the triad, invariably come to light and the discussion is general, active, and helpful. On one occasion it lasted for one hour and in another meeting for one hour and thirty minutes. When obstetric programs can provoke discussions for that length of time, they are fulfilling a very large part of their mission.

This plan of district meetings has met with the splendid cooperation of the officers of the various societies contacted. It has been more a question of finding time to put on all the programs requested than of creating a demand for them. Since January, 1936, when the committee first began to put on these programs, we have appeared before five district societies. At the present rate of progress, it will take us more than a year to fill all the remaining requests for meetings.

It is obvious to us that our State Committee can function best only as a directing agency and as a clearing house and that the most effective work will be done by the district societies. To further this, we are asking that each district society appoint a subcommittee on maternal welfare. We recommend that each subcommittee consist of three physicians, at least one of whom shall be a rural practitioner. We expect such subcommittees to: (1) Sponsor obstetric programs in their own societies at stated intervals. (2) Encourage case reports in obstetrics by the society members. (3) Foster educational work among lay organizations such as Federated Women's Clubs, Parent-Teachers Organizations and Home-Makers Clubs.

Other activities of such committees naturally suggest themselves, but it has seemed wise not to burden these committees with too extensive a program at the

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WILLIAM J. DIECKMANN, M.D.

Editorial Comment

The Induction of Premature Labor in Contracted Pelvis

THE induction of premature labor for moderate degrees of pelvic contraction is one of the deep-rooted traditions of British obstetrics. It dates, as Denman points out, from about 1756 when a group of London physicians, seeking a substitute for craniotomy in cases of contracted pelvis, met "to consider of the moral rectitude of, and advantages which might be expected from this practice." There can be no doubt that the contributions of British obstetricians to this general field have had far-reaching and beneficial effects. Today the induction of premature labor is recognized the world over as a valuable measure in the treatment of many obstetric conditions. Oddly enough, however, its use in the complication it was originally designed to serve, contracted pelvis, is at present confined almost entirely to Great Britain.

Recent evidence suggests that even in Great Britain opinion is veering away from this practice. There appears in the September, 1936, *Proceedings of the Royal Society of Medicine* a significant symposium on the motion, "That induction of premature labour should not play any part in the treatment of contraction or disproportion in primigravidae." Seventeen leading obstetricians discussed the proposal and the majority (10) favored the motion, that is, opposed the induction of labor for contracted pelvis. Their statements were based on series of cases from various English hospitals and referred in most instances to inductions brought about by means of bougies. During the discussion even the advocates of the method conceded a fetal mortality of 12 per cent, or more. Induction of premature labor in primigravidas at King's College Hospital resulted in a stillbirth rate of 20.8 per cent. At St. Thomas's Hospital and the General Lying-In Hospital, York Road, the infant mortality following the same measure was 16.5 and 17.5 per cent, respectively. Uterine inertia and infection were not infrequent sequelae. At the Middlesex Hospital, where labor was induced prematurely in 44 primigravidas because of disproportion, uterine inertia occurred in 38 per cent. The induction of premature labor at the King's College Hospital increased the forceps rate no less than threefold, while 45 per cent of the patients showed definite evidence of uterine infection after delivery.

That certain British obstetricians have definitely abandoned premature induction of labor in contracted pelvis, seems clear. Of interest to

nancy," "Mode of Living for the Pregnant Woman," "Common Disorders of Pregnancy," "Danger Signs of Pregnancy," "Puerperal Infections," and "The Toxemias of Pregnancy." Because of the response to this feature of lay education, it was decided to prepare and broadcast a series of four talks on Infant Welfare. The subjects to be covered are: "The Newborn Infant," "Breast Feeding," "The Infant in the First Few Months of Life," and "Immunization."

Every radio program must have a "radio signature" or a "theme song." Ours is "See Your Doctor!" Throughout all our talks we have repeatedly urged the importance of the personal relationship between patient and physician. We have not attempted any "question and answer" department, any advice by mail or any of the other follow-up procedures usually associated with radio broadcasting. If we have succeeded in awakening any public interest in the field of maternal welfare, we have obtained our objective and the patient and her private physician are the beneficiaries.

Home-Maker Clubs are very active in North Dakota. They are well organized and interest in them is high. Regular courses of study are followed and the assignments are made well in advance of the scheduled meetings. Our committee was approached by the State Department of Health as to the possibility of providing a course of study, dealing with maternal and infant welfare, for Home-Maker Club meetings. The response of the committee was unanimously in favor of such a plan, and we expect to assist in the preparation of such a course of study in the very near future.

Whatever may be our individual attitudes toward Social Security Legislation, I believe we all realize that, in some form or other, it is here to stay. The attitude of the medical profession in North Dakota, as I have been able to determine it, is decidedly against socialized medicine. The first thing our committee did was to assure our medical audiences that our program was the antithesis of state medicine or socialized medicine in any form. When our physicians understood that, in our program for maternal and infant welfare, we were representing organized medicine in North Dakota and that we were a regularly appointed committee of the North Dakota State Medical Association, cooperation supplanted whatever skepticism might have been present.

As our committee sees it, our problem is to develop its state program along lines which will increase the prestige of the individual practitioner of medicine and bring our influence to bear with state health officials to further that end. We have stressed and will continue to stress, both to medical and lay audiences, the personal relationship which must exist between patient and physician to improve the standards of obstetric practice. All the members of our committee are men engaged in the private practice of obstetrics and/or gynecology. Doctors in North Dakota are highly individualistic and I, for one, hope that they remain so. It is not regimentation we are looking for but cooperation. I believe that our influence, as a committee, will be felt in the development of state plans for maternal and child welfare in North Dakota. I have indicated some of the projects under way and some of our plans for the future. We believe that only through the cooperation of the physicians of the state and the education of the patients to seek the highest type of obstetric service available to them can this, or any other, program of maternal welfare succeed. We are cooperating with the Public Health Officer in planning and supervising a program of maternal and child welfare, and we are doing so as private practitioners. If we can continue the cordial relationships now being established between organized medicine on the one hand, and a rapidly developing state plan for maternal welfare on the other, our efforts will succeed. The response to date has made us optimistic for the future.

Society Transactions

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF OCTOBER 1, 1936

The following papers were presented:

The Primiparous Internal Genitalia After Forceps Delivery. Dr. Fred B. Nugent. (For original article, see page 611.)

Use of Parathyroid Extract for the Control of Early Nausea and Vomiting of Pregnancy. Dr. Walter Sussman. (To appear in a subsequent issue.)

The Incidence of Ureteral Stricture in Lower Abdominal Pain in Women. Dr. Charles Lintgen. (For original article, see page 636.)

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF APRIL 3, 1936

The following papers were presented:

The Diagnostic Value of the X-Ray in Placenta Previa. Drs. S. C. Hall, F. W. Currin and J. F. Lynch. (For original article, see page 625.)

MEETING OF NOVEMBER 6, 1936

The following papers were presented:

Abdominal Pregnancy. Diagnosis Confirmed by Hysterography. By Dr. A. Louis Friedman. (For original article, see page 683.)

A Report on Radiation Treatment of Cancer of the Corpus and Cervix Uteri. By Dr. William S. Smith. (For original article, see page 596.)

Congenital Atresia of the Esophagus With Tracheo-Esophageal Fistula. By Dr. Alexander R. Rosenthal. (For original article, see page 646.)

American obstetricians is the fact that this reversal of attitude is said to be the result of a statement made by the late Dr. J. Whitridge Williams when he visited England in 1925. Since 70 to 80 per cent of all labors complicated by contracted pelvis end spontaneously if treated expectantly, Williams held that the induction of premature labor is rarely justified and that in cases of moderate pelvic contraction equally good results for the mother, and far better results for the child, are obtained by abstaining from it, and subjecting to cesarean section at term all patients who present such disproportion as makes a spontaneous outcome unlikely. The principal difficulty connected with the induction of labor in such cases, he pointed out, is to recognize those which will require it, and to choose the correct time for its performance. Failing to do these things, and it is utterly impossible to carry them out with precision, two pernicious results will ensue. On the one hand, many patients will be induced unnecessarily, while on the other, certain women will fail to deliver even premature infants. In the latter instance the patient has obviously been rendered unfit for cesarean section by the instrumental induction and both her life and that of her child placed in jeopardy. In the recent symposium, Mr. A. J. Wrigley cites evidence to show that in England "over the last few years thousands, possibly tens of thousands, of unnecessary inductions have been performed."

But it must be emphasized that the verdict of the symposium was not unanimous. Seven of the seventeen obstetricians supported the induction of premature labor and adduced evidence to show that the fetal mortality of this procedure is no higher than that of trial labor. They rightly feel that "the operation of caesarean section is treated much too lightly and performed far too often" in moderate degrees of contracted pelvis. Again Williams' name comes into the discussion but now unfavorably as the sponsor of the "anti-induction school of thought" in England. He is criticized in particular by Dr. Herbert Spencer on the grounds that "Professor Whitridge Williams' personal experience of induction for contracted pelvis was limited to one case." For some thirty-five years Williams' principal clinical interest was the course of labor in contracted pelvis and few other men have had the opportunity to observe such rich material in this field. The induction of premature labor for certain complications of pregnancy he, of course, practiced frequently. Moreover, as his textbook shows, he had weighed carefully the results of this procedure in contraction of the pelvis, as reported by Kleinwächter, Pinard, Bar and others and, in brief, found them inferior to those obtainable by other methods. With such a background "one case" might prove ample.

If the premature induction of labor for contracted pelvis is losing ground in England, the change will be watched with interest in this country. Certainly, it is one of the few subjects on which American obstetricians could take serious issue with their British colleagues.

Nicholson J. Eastman.

Cuilla, A.: *The Arterial System of the Placenta*, *Folia gynaec. Demograph.* 31: 641, 1934.

By using x-ray opaque substance the author has studied the arterial system of the placenta. He found the normal placenta at term so consistently of the same arterial structure that the diagnosis of albuminuria, eclampsia and syphilis is easily made, without any other study necessary. The picture presented by the placenta is pathognomonic.

MARIO A. CASTALLO.

Peckham, C. H.: *A Statistical Survey of 186 Cases of Manual Removal of the Placenta*, *Bull. Johns Hopkins Hosp.* 56: 224, 1935.

The incidence of manual removal of the placenta in women delivered at or near term at the Johns Hopkins Hospital from 1896 to 1933 was 1 in 120 cases. This operation was necessary much oftener in white than in black patients delivered in the clinic. It also was performed more commonly in multiparas and in women during the older age periods of their childbearing careers. The incidence of manual removal was higher following prolonged labor and was particularly common in multiparas delivered spontaneously after a long labor due to uterine inertia. Manual removal was necessary much more frequently following premature than term delivery.

Hemorrhage was the most common indication for the procedure and retention of the placenta the least common. In about one-third of the cases a previous obstetric operation with a desire to terminate promptly the third stage was the indication for manual removal.

The gross morbidity rate, excluding patients dying within forty-eight hours of delivery, was 54.95 per cent. After spontaneous delivery, and where manual removal was the only manipulation, in 48.48 per cent of the patients there followed a febrile puerperium. The gross maternal death rate was 10.75 per cent and that due to sepsis 3.23 per cent. In cases where delivery was spontaneous, the above two rates were 10.45 and 4.48 per cent, respectively.

The operation of manual removal of the placenta has its definite indications but its employment should be limited. Intelligent care of the patient during the third stage of labor will lower its incidence by preventing partial separation.

C. O. MALAND.

Rosenfeld, S. S.: *The Management of Abruptio Placentae*, *Am. J. Surg.* 21: 279, 1933.

This condition is frequently found in association with low implantation of the placenta. The case is then characterized by the signs and symptoms of both conditions. In the author's series of 15 cases toxemia was present 12 times, eclampsia once. The hemorrhage associated with this condition is either concealed or apparent. It may remain concealed under the following conditions: (1) when there is an effusion of blood behind the placenta, its margins still remaining adherent; (2) when the placenta is completely separated while the membranes retain their attachment to the uterine wall; (3) when blood gains access to the amniotic cavity after breaking through the membranes, and the amniotic sac remains intact below; and (4) when the head is so actively applied to the lower uterine segment that the blood cannot make its way past it. The symptoms as a rule depend on the severity of the bleeding and the amount of shock. The blood pressure is usually elevated, and the urine contains albumin. In the severe cases all the signs and symptoms are marked. There is usually a sudden onset with very severe abdominal pain, a profound degree of shock, and a semicomatose or even a completely comatose state

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

PLACENTA

Frey and Forster: Uterine Contractions in the Placental Period, *Ztschr. f. Geburtsh. u. Gynäk.* 107: 311, 1934.

With the aid of the hysterotonograph, a new instrument for registering both contractions and tonus of the uterus, it is convincingly shown that the expulsion of the fetus is not followed by a rest period of uterine activity as heretofore assumed. The first contraction of the placental stage begins anywhere from a few seconds to three and one-half minutes after expulsion of the child. The frequency of the contractions averages 3.5 per ten minutes. The placental period was terminated by 6 to 10 contractions in 95 per cent of all patients; only a very small percentage required from 11 to 15 pains; 75 per cent were ended with 5 contractions.

The expulsion of the child is followed immediately by a marked decrease of uterine tonicity. Both the duration of each contraction and the tonicity of the uterus are important factors in the time necessary to conclude the placental stage.

Blood loss is dependent upon the number of contractions necessary to end the placental stage. It amounts to only 100 gr. or less when only few contractions are required.

GROVER LIESE.

Scheibel, O.: The Influence of Pitocin on the Delivery of the Placenta, *Acta obst. et gynec. Scandinav.* 15: 211, 1935.

The author found that in a series of 300 primiparas 11 per cent lost more than 400 gm. of blood. He administered 5 units of pitocin in 300 other women and ascertained that only 4 per cent of these women suffered a similar loss of blood. No untoward complications were observed from the use of pitocin.

J. P. GREENHILL.

Kraistensen, B.: Manual Detachment of the Placenta and Intrauterine Palpation, *Acta obst. et gynec. Scandinav.* 15: 165, 1935.

Previously intrauterine manipulations after delivery were considered to be dangerous. Recent experience, however, has convinced Kraistensen that these dangers have been exaggerated. To prove this he collected the cases of intrauterine manipulation in the Maternity of the Copenhagen State Hospital from 1924 to 1933. He found that among 16,137 labor cases the uterus was invaded 208 times. Analysis shows that intrauterine manipulations were dangerous only in patients who were infected or markedly anemic. The author advises exploration of the uterus for removal of a placenta as early as possible. In uncomplicated cases the risk is slight.

J. P. GREENHILL.

Up to 1927 the treatment was almost exclusively obstetric, but since that year, the low cervical cesarean section has been employed in the serious cases. Since 1932, hysterectomy has been reserved for the graver cases. In the entire series of 59 cases there was only one maternal death (1.7 per cent) and this patient died from bronchopneumonia following a Braxton Hicks version. Among the 49 patients treated obstetrically, the mortality was 2 per cent, whereas of the 10 patients treated surgically, all survived. The latter operations consisted of two classic cesarean sections, 4 cervical operations, and 4 Porro operations. The fetal mortality among the patients treated obstetrically was 51.2 per cent and for those treated by surgical means it was 50 per cent.

Not a single patient in this series was transfused. The authors consider it illogical and dangerous to perform a blood transfusion before the bleeding is checked. On the other hand, when the hemorrhage is controlled, recovery is so rapid that transfusion is unnecessary.

J. P. GREENHILL.

Reeb: The Treatment of Placenta Previa in the Strassburg Obstetric and Gynecologic Clinic From 1920 to 1932, *Bull. Soc. d'obst. et de gynéc.* 1: 106, 1933.

During the years 1920 to 1932 there were 101 cases of placenta previa in the Strassburg clinic among 18,307 labor cases (0.55 per cent). There were 91 multiparas and 10 primiparas. In 91 cases there were signs of labor at the time the bleeding occurred.

The treatment was obstetric in 61 cases and surgical in 35 cases. In five cases the obstetric therapy failed, so surgery was employed. Rupture of the bag of waters was performed 8 times without any maternal mortality. A rubber balloon was used 20 times with two maternal deaths. Among 11 Braxton Hicks versions there were no deaths but among the 18 versions and extractions 5 mothers succumbed. Among the 61 patients treated obstetrically, 8 mothers (13 per cent) and 35 infants (57.3 per cent) died.

Surgical treatment is divided into vaginal hysterotomy, classic cesarean section, the low cesarean section, and subtotal hysterectomy. The cervical operation is the one of choice, for it was performed 32 times since 1922 and only 1 mother and 6 infants died. The ideal anesthetic is by the spinal route.

J. P. GREENHILL.

Keller, R.: The Results of Treatment of 100 Cases of Placenta Previa Observed at the Maternité From 1920 to 1932, *Bull. Soc. d'obst. et de gynéc.* 1: 112, 1933.

Among 19,898 labor cases observed at the Strassburg Maternité there were 100 cases of placenta previa. Of these, 88 were delivered vaginally and 12 by cesarean section. Among those treated obstetrically the maternal mortality was 6.8 per cent and the fetal death rate was 54.5 per cent. On the other hand among the 12 cesarean sections, there were no maternal deaths and only 1 infant died. Hence, the indications for cesarean section in cases of placenta previa should be extended in the future.

J. P. GREENHILL.

Brémond: Placenta Previa and Medical Induction of Labor, *Bull. Soc. d'obst. et de gynéc.* 4: 364, 1933.

The method of treating placenta previa advocated is that recommended by Fournier and is as follows: Four doses of quinine are given at half hourly intervals. These are followed by eight injections of pituitary extract administered every half hour, beginning at the time of the last dose of quinine.

J. P. GREENHILL.

and an extremely tender and hard ligneous, boardlike uterus. In the mild cases the fetal heart can usually be heard, and a living fetus is frequently delivered, while in the graver cases the fetal heart as a rule cannot be elicited and the infants are most frequently stillborn. Postpartum hemorrhage is a frequent complication; the prognosis is always serious.

The plan of procedure to be adopted will depend upon certain obstetrical factors. The general indications are to empty the uterus and control the hemorrhage. Transfusion, before any operative procedure is undertaken, is of paramount importance. The author generally performs cesarean section under local infiltration anesthesia.

J. T. WITHERSPOON.

Gigon, C.: Four Cases of Uterine Apoplexy, *Bull. Soc. d'obst. et de gynéc.* 25: 225, 1936.

The author reports 4 cases of uterine apoplexy. He does not believe that all such cases must necessarily be treated by hysterectomy. Where the uterus can be conserved, he favors the classical cesarean section rather than the cervical one because it is simpler, it can be performed more rapidly, it has less postoperative morbidity, and also because it permits exteriorization of the uterus to verify the extent of the lesion in the uterus. In 3 of his 4 cases there was marked albuminuria.

J. P. GREENHILL.

Cathala, D.: The Treatment of Retroplacental Hemorrhage With Uterine Apoplexy, *Bull. Soc. d'obst. et de gynéc.* 24: 322, 1935.

At the Maternity of the St. Louis Hospital in Paris, among 59,500 deliveries, there were 5 deaths which resulted from retroplacental hemorrhage. Three of these women died after hysterectomy, one after spontaneous labor from hemorrhage, and the other after forceps delivery from infection. During the last few years there has been an increase in abdominal deliveries for abruptio placentae in the author's clinic. However, obstetric intervention has yielded better results than hysterectomy, hence the author feels that vaginal delivery in the presence of retroplacental hemorrhage with uterine apoplexy is frequently indicated. The prognosis in these cases depends chiefly upon the state of shock which is present. The best method of intervention is that which least aggravates the shock. A destructive operation upon the child, if performed rapidly without trauma to the mother, without anesthesia or with a minimum of anesthesia, is less harmful to the mother than a hysterectomy. This is why a delivery from below frequently gives better results than an abdominal operation.

A hysterectomy after a cesarean section gives better results than a hysterectomy without previous removal of the child. Hysterectomy is the operation of choice when the cervix is not dilated or not sufficiently dilated to permit the extraction of the child whose size is reduced by a destructive operation.

J. P. GREENHILL.

Andérodias, J., and Mahon, R.: The Treatment of Placenta Previa at the Bordeaux Obstetric Clinic from 1920 to 1932, *Bull. Soc. d'obst. et de gynéc.* 6: 510, 1933.

Among 11,078 labor cases at the Bordeaux Obstetric Clinic there were 59 cases of placenta previa (0.53 per cent). Of this number, 14 (24 per cent) were primiparas and 45 (76 per cent) were multiparas. In 40 cases the bleeding began during pregnancy and in the remainder after start of labor.

section. After considering the manner of delivery and the higher percentage of fatalities both to mothers and babies by methods other than cesarean section, the author makes a plea for the more frequent use of this operation in cases of placenta previa.

MARIO A. CASTALLO.

Klein, S. M.: *The Treatment of Placenta Previa*, Monatschr. Geburtsh. u. Gynäk. 99: 170, 1935.

At the Woronench Woman's Clinic, from 1925 to 1933, there were 59 cases of placenta previa among 11,866 labor cases. Only 9 per cent of these occurred in primiparas. Klein found that placenta previa occurred among women who had abortions ten times more frequently than among women who did not have abortions. Most of the patients delivered after artificial rupture of the membranes and Braxton Hicks version. Among the 30 women so treated, 16.1 per cent of the mothers and 79.4 per cent of the babies died. On the other hand, among 10 women delivered by classic cesarean section, no mother died but 22 per cent of the babies succumbed. Hence the author is convinced that the surgical treatment of placenta previa by cesarean section is far preferable to delivery from below. In the home, however, best results will be obtained by means of Braxton Hicks version or the insertion of a colpeurynter. After the use of these methods delivery of the child must be spontaneous in order to avoid lacerations in the cervix.

J. P. GREENHILL.

Browne, O'Donel: *Methods at Present Used in the Treatment of Placenta Praevia*, Irish J. M. Sc. 2: 540, 1936.

The incidence of placenta previa is approximately one in every 150 full-term pregnancies. It occurs frequently at or before the twenty-fourth week, being the unsuspected cause of many miscarriages. The condition is diagnosed by identifying the placenta on vaginal examination. The variety of placenta previa is determined during this examination.

The author collected figures from the reports of four well-known maternity hospitals in England and Ireland. The gross maternal mortality from all causes attributable to, or associated with, placenta previa was 4.5 per cent. The gross fetal mortality in the same series was 56.5 per cent. Treatment and results in the three types are discussed. The author concludes that (1) Revision of our present treatment would improve the fetal and maternal results. (2) At the present time cesarean section is not used with sufficient frequency in the treatment of placenta previa. (3) Simple puncture of the membranes offers the best combined fetal and maternal results in lateral and marginal placenta previa. (4) Bipolar version should be reserved for the actively bleeding and exsanguinated cases, particularly when the central placenta previa is encountered in general practice.

F. L. ADAIR AND S. A. PEARL.

Laffont, A., and Fulconis, A.: Placenta Previa at the Algerian Maternity, *Rev. franç. de gynéc. et d'obst.* 29: 189, 1934.

Among 11,921 labor cases at the Algerian Maternity there were 301 cases of placenta previa. Among these, 281 were treated as follows: rupture of the membranes 110 times, rupture of the membranes, bag or version without immediate extraction 95 times, internal version after complete dilatation 73 times, and the Delmas procedure 3 times. Of these 281 cases 18 women died (6.4 per cent). The causes of death were hemorrhage in 5 cases, rupture of the uterus in 7, infection in 4, embolism in 1, and shock in 1 case. Since 1924, six classical cesarean sections have been performed with two deaths and twelve cervical cesarean sections without any maternal mortality.

The authors conclude that obstetric treatment should be used in marginal cases of placenta previa especially where labor seems to progress normally after rupture of the membranes. Cesarean section should be employed where there are mechanical difficulties, abnormal presentations, large babies and contracted pelves. If after rupture of the bag of waters, the hemorrhage does not cease, or the presenting part remains high, or dilatation of the cervix does not progress, the authors likewise recommend cesarean section. They prefer the cervical operation and employ spinal anesthesia provided the blood pressure permits its use. They believe preoperative transfusion to be a very helpful procedure.

J. P. GREENHILL.

Essen-Möller, E.: Experiences and Historical View Point of the Treatment of Placenta Previa, *Acta obst. et gynec. Scandinav.* 13: 195, 1934.

The author analyzes 245 cases of placenta previa. Of these, 96 (39.3 per cent) were delivered after either spontaneous or artificial rupture of the membranes, with only 1 death. Version was performed in 72 cases, with 5 deaths, and, adding 6 cases of breech presentation with 1 death, the result was 78 cases with 6 fatal issues (7.6 per cent). Thirty-three cases were dealt with by abdominal, and another 33 by vaginal cesarean section, with 1 and 3 fatal issues, respectively. Together there were 66 cases with 6.06 per cent mortality.

The results as regards the child were 29.2 per cent mortality after artificial rupture of the membranes, 64.6 per cent after version and 17.9 per cent after cesarean section. Deducting the children under 2,000 gm. and those dead before intervention, the respective figures are 9.7, 55.8, and 3.5 per cent.

Discussing the various methods, the author comes to the following conclusions. He rejects plugging of the vagina and metrectomy. In the majority of cases of lateral placenta previa, puncture of the membranes is quite sufficient. Version still maintains its place where the mother is delivered in her home, or if the child is dead; but it gives bad results as regards the child, and yet cannot give good results as regards the mother. In many cases, abdominal cesarean section is therefore justified, but the author refuses to adopt it as the method for all cases. Vaginal cesarean section may be performed in exceptional cases, for instance if infection is suspected, or if imminent danger of life makes it urgent to deliver the patient at once and that method seems the easiest way of doing so.

The author strongly insists that a patient with placenta previa should be transported to a maternity hospital as soon as possible after the appearance of the hemorrhage.

J. P. GREENHILL.

Garofalo, Agostino: A Consideration of 247 Cases of Placenta Previa, *Folia gynaec.-demograph.* 32: 229, 1935.

The author reviews 247 cases of placenta previa occurring in the Clinic of Palermo from 1923 to 1934. Among the group there were 48 patients delivered by cesarean

Items

American Board of Obstetrics and Gynecology

Practical oral-clinical, and pathological examinations for Group A and Group B applicants will be held at Atlantic City, N. J., on June 7 and 8, 1937.

An informal dinner for the Diplomates of this Board and others interested in obstetrics and gynecology will be held at the Hotel Claridge, Atlantic City, on Wednesday, June 9, 1937, at 7:00 P.M. At this time several short addresses will be made and the successful candidates of the preceding two days' examinations will be introduced in person.

Applications for the Group A examination will be received in the office of the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa., to April 9, 1937. Application blanks may be secured from the Secretary's office.

Pacific Coast Society of Obstetrics and Gynecology

The next meeting of the Pacific Coast Society of Obstetrics and Gynecology will be held in San Francisco, November 3 to 6, 1937 at the Fairmont Hotel.

American Committee on Maternal Welfare, Inc.

The American Committee on Maternal Welfare, Inc., will have a luncheon meeting at the Hotel Dennis in Atlantic City, N. J., on Wednesday, June 9, at 12:15 P.M. Short addresses will be made by Dr. Malcolm T. MacEachern, Dr. H. G. Weiskotten, and Dr. Ray Lyman Wilbur. An invitation is extended to those interested in maternal welfare activities.

Correspondence

CASE OF TRIPLE PREGNANCY DIAGNOSED BY X-RAY

As pointed out in an article on this subject by Dr. Margaret B. Ballard, which appeared in the August, 1936, issue of the JOURNAL, a diagnosis of triplets before delivery is infrequent. She stated that the review of the available literature revealed only nine cases. Ballard gives a brief description of these cases, and details a case of her own. Greenhill, in a letter to the Editor, published in the November, 1936, issue of the JOURNAL, mentions a case he reported in 1923 in which the correct diagnosis was not made until the x-ray plates were re-examined after delivery.

I wish to add a case of triple pregnancy diagnosed by means of the x-ray before delivery, which occurred in my practice recently.

Mrs. I. A., white, aged twenty-five years, married four years, para 0. The family history was irrelevant. The past history of the patient was negative. There had been no multiple pregnancy in the family of the patient or the husband's family. The date of onset of her last menstrual period was March 8, 1936. The patient was first seen by me June 17, 1936. Examination at this time revealed a fundus much larger than normal at this period of pregnancy. Frequent cramplike pains were complained of. The pregnancy continued without definite trouble, rapid enlargement of the abdomen being noted, and when the seven-month period was reached, the height of the fundus corresponded to full term, the abdomen was quite tense, and marked hydramnios was present. It was not possible to palpate fetal parts or hear fetal heart sounds at this time. Multiple pregnancy or fetal anomaly was suspected, therefore an x-ray examination was requested. This was done by Dr. Isadore Lattman of the Garfield Memorial Hospital, and he reported Oct. 16, 1936, the presence of triplets. There had been a total weight gain of thirty-six pounds, blood pressure remained normal throughout pregnancy and the patient kept active. Labor began spontaneously Oct. 25, 1936, at 11:30 P.M., approximately seven weeks prematurely. There had been an escape of amniotic fluid for twenty-four hours just preceding onset of labor. The progress of the labor was rapid and under nitrous oxide anesthesia, a median perineotomy was done, and at 6:04 A.M., Oct. 26, 1936, the first baby was delivered, the position persistent R.O.P. The second bag of waters was ruptured artificially and the second baby, which was L.S.A. position, was delivered by extraction at 6:09 A.M. The third sac was now artificially ruptured, and with moderate pressure on the fundus, the occiput appeared at outlet and was delivered at 6:14 A.M. as an L.O.A. The placenta was expressed at 6:25 A.M., and the perineotomy wound sutured. The placenta was normal appearing. The cords were centrally inserted. Three amniotic sacs and one chorion were noted. All of the babies were females and weighed three pounds twelve and one-half ounces, three pounds one ounce, and three pounds twelve ounces, respectively.

The babies were given the usual premature care. Mothers' milk from wet nurses was secured, and they are, at three months of age, healthy and vigorous babies, having gained more than five pounds each. I desire to express my appreciation of the excellent care these infants received under Dr. H. H. Donnally, the pediatricist in charge of them.

E. W. TITUS, M.D.

Washington, D. C.

the amount of the drug administered but also upon the type of barbiturate given. In experimental animals barbital and phenobarbital produce anesthesia lasting from seven to thirteen hours, amytal two to seven hours, ortal and pentobarbital one to two hours, and evipal, thio-pentobarbital and thio-ethamyl only fifteen to thirty minutes. The duration of this effect can be modified by certain changes in the body. Hirschfelder and Haury³ have shown that nephrectomy lengthens this action for phenobarbital and barbital from eleven to thirteen hours to thirty-six and seventy-nine hours, respectively. This operation has no effect upon the duration of action of amytal, pentobarbital, ortal, and evipal.

We⁴ studied the effect of nephrectomy upon the duration of anesthesia produced by ortal sodium in dogs. In these there was no change. Liver damage, however, lengthens the actions of the short acting group. It is evident from these results that the effects of the former two drugs, since they are eliminated by the kidney, would be lengthened in nephritic patients, whereas the latter, amytal, ortal, etc., which are probably destroyed by the liver, would show increased duration of anesthesia in cases with liver damage. Recently some evidence has been presented to show that all barbiturates including amytal and pentobarbital are excreted by the kidneys.⁵ This has been denied by others⁶ who have shown that probably only degradation products appear in the urine following anesthetic doses of amytal, pentobarbital, and ortal.

The rapidity with which the latter drugs leave the circulation when injected intravenously was shown by Brundage and Gruber.⁷ One to seven minutes after the intravenous injection of anesthetic doses of these drugs only 2 to 5 mg. per 100 c.c. of blood was observed, i.e., only about $\frac{1}{10}$ of the amount injected intravenously remained in the entire circulation one to seven minutes after their injection. This level was maintained until the animal came out from under the anesthetic one to three hours later. This seems to show that these drugs are stored in some tissues of the body and for some time thereafter they are given back to the blood stream as fast as they are destroyed by the liver. The total amount of these degradation products excreted in the urine varies considerably with different barbiturates in different animals. In our investigation as small amounts as 2.4 to 7.5 per cent of the sodium salts of amytal and ortal may appear in the urine upon their intravenous injection. However, as much as 22 per cent of the sodium pentobarbital may be found in the urine during the same period. The substance excreted, however, as far as we could determine is not the barbiturate. The intraperitoneal injection of this excreted material into mice produces neither hypnosis nor anesthesia.

One of the objectionable features of all barbiturates in obstetrics is the high percentage of cases showing extreme restlessness and maniacal symptoms. Some of these patients require restraint for delivery. Some clinicians report one-third of their patients markedly restless and one-

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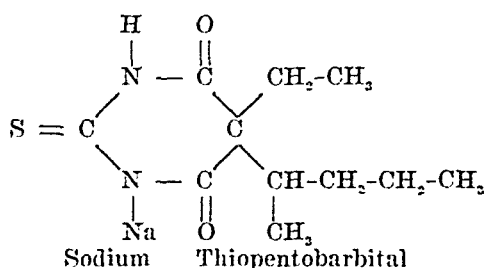
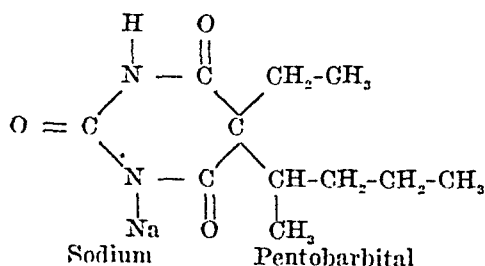
Original Communications

ON CERTAIN PHARMACOLOGIC ACTIONS OF THE NEWER BARBITURIC ACID COMPOUNDS*

CHARLES M. GRUBER, M.D., PHILADELPHIA, PA.

(From the Department of Pharmacology, Jefferson Medical College)

THE clinical usefulness of the barbituric acid derivatives in obstetrics can best be evaluated and discussed by obstetricians who have had clinical experience with these drugs. Suffice it to say that some writers claim excellent, others unfavorable clinical results with the same drug.¹ Today the obstetrician is confronted not only by one but by many barbiturates and to make things more complicated a second series, the thioderivatives, have recently been introduced into medicine.² As we shall point out in this paper, the substitution of sulphur for the oxygen in the malonyl urea ring has changed the actions of the drug enormously.



All barbiturates when administered orally, rectally, intramuscularly, or intravenously produce varying stages of hypnosis, narcosis, or anesthesia and even death. The effect obtained is dependent not only upon

*This investigation was made possible principally by a grant from Parke, Davis and Co., to the Jefferson Medical College for research in science.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

ortal, evipal, and thiopentobarbital. In some animals evipal and thiopentobarbital do not produce narcosis but convulsions. In our studies¹⁵ on rats, we employed a sudden mechanical stimulus to the tail instead of the slow pressure stimulus as outlined by Eddy¹⁶ for eliciting the degree of anesthesia. In these, evipal and thiopentobarbital did not abolish reflexes unless morphine sulphate was added. In some animals, evipal was administered in toxic doses, yet the animal responded by a sudden contraction of the skeletal muscles upon sudden pressure applied to the tail, ear, or foot. We were also unable to produce anesthesia in the majority of the rabbits studied upon the intravenous injection of evipal and thiopentobarbital. Cessation of respiration usually occurred before anesthesia could be produced.

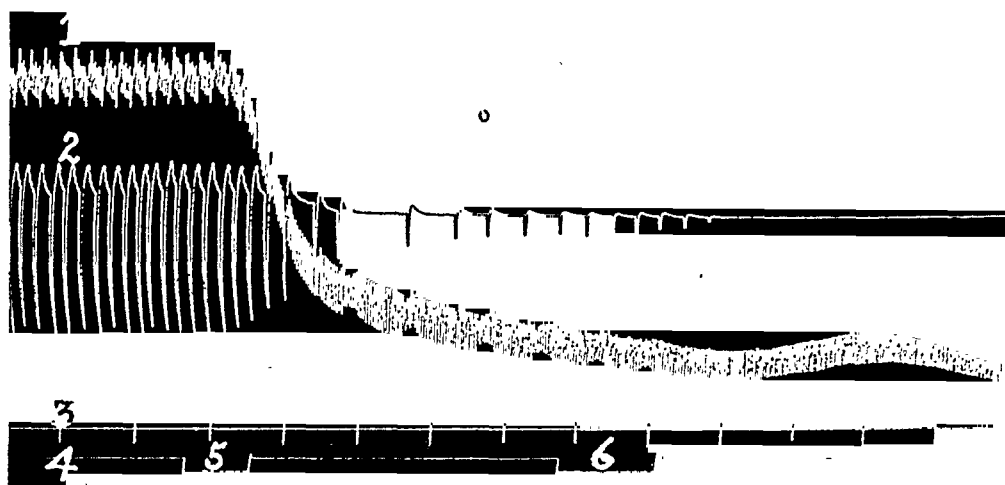


Fig. 2.—Dog, 9.5 kg. Paraldehyde anesthesia. 1, Blood pressure with mercury manometer. 2, Respirations recorded with pneumograph. Down stroke in the record is that of inspiration. 3, Time in fifteen seconds and writing point at atmospheric pressure. 4, Duration and time of injection of 400 mg. of sodium phenobarbital intravenously (at 5). Caffeine sodiobenzoate injected (at 6). Record shows complete cessation of respiration before the heart ceased beating.

In addition to hypnosis and anesthesia all of these drugs depress the respiratory center and death may result¹⁷ (see Figs. 1 and 2). Since the respiratory center is affected before the cardiovascular system, there is always a possibility of using artificial respiration and thus preventing a catastrophe.

It has been shown in pregnant dogs¹⁸ and rats¹⁹ that these drugs pass freely from the mother through the placenta to the fetus and back again into the mother's circulation. Jaroschka²⁰ found barbiturate in the urine of two dead fetuses following the use of pernocton in the delivery of the mothers. It is apparent, therefore, that infants born of mothers under deep barbiturate anesthesia may show some difficulty in establishing spontaneous respiration.²¹ Some authors report one-third of the babies as apneic at birth with difficult resuscitation. Others cite even stillbirths. Averett²² reports the fact that in his series, 8 babies required resuscitation, upon the use of nembutal and scopolamine in the mothers. Bohler¹⁰ reports 3 babies narcotized following the use of pernocton in 102 obstetric cases, and Galloway

third moderately restless.⁸ Ruth and Paxson⁹ record this restlessness due to the use of amytal as a disadvantage. Similar objections were voiced by Bohler¹⁰ and Olson and Van Ess¹¹ with the use of pernocton,

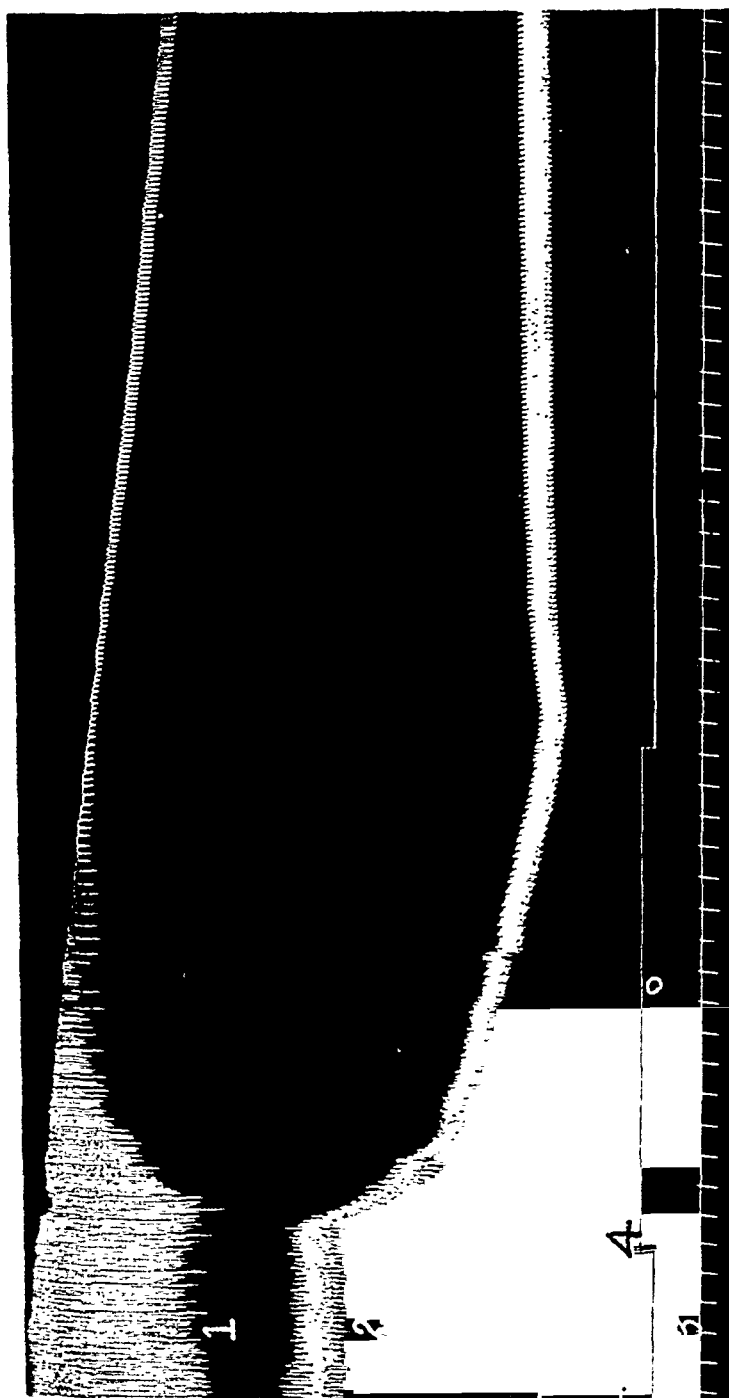


Fig. 1.—Dog, 11 kg. Light ether anesthesia. 1, Respiration with a pneumograph about the upper abdomen and the thorax. Down stroke is that of inspiration. 2, Blood pressure from the carotid artery taken with a mercury manometer using heparin as the anticoagulant. 3, Time in ten seconds and zero blood pressure. 4, Duration and time of injection of 600 mg. of sodium amytal intravenously. There are noted a marked fall in the general blood pressure and a decrease in the rate and depth of respiration, both returning to normal seventy-five minutes later.

and Galloway and Smith¹² and Boylan¹³ with pentobarbital. Most obstetricians report the production of amnesia in the majority of patients treated with barbiturates.¹⁴

A corresponding period of excitement before the production of anesthesia is noted in experimental animals with amytal, pentobarbital,

the Cushny myocardiograph²³ applied to the heart (Fig. 3) and by experiments with perfused excised hearts.²⁴ Complete cessation of contraction of the excised monkey's heart when perfused with evipal was shown by Storm. All of the ordinary barbiturates depress the peripheral vagus nerve endings, and a stronger stimulus is required to inhibit the heart. This is readily shown upon electrical excitation of

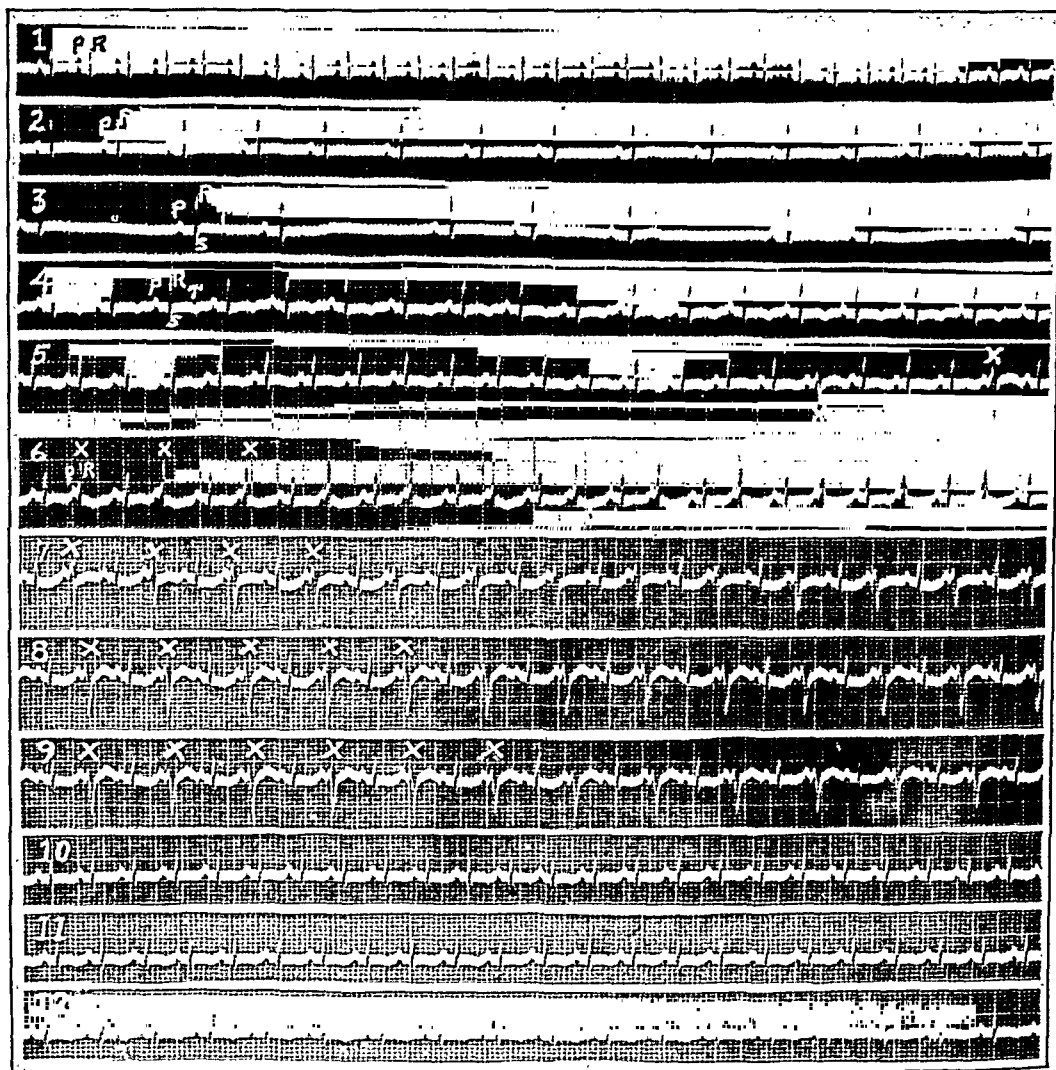


Fig. 4.—An electrocardiogram taken in a dog weighing 11.8 kg. Records taken before and after injections of morphine sulphate and sodium pentothal. Lead II. 1 mv. = 1 cm. Res. 2000 ohms. Controls 1 and 2. Record 1 was taken during a period of playful excitement and 2, five minutes later after the animal had become quiet. The animal was then given 5 mg. per kg. of morphine sulphate subcutaneously. Record 3 was taken fifty-four minutes after the injection of morphine. Sixty-two minutes after the injection of morphine 236 mg. of pentothal sodium (20 mg. per kg.) were injected intravenously. Duration of injection was four and one-half minutes. The respirations were good throughout the experiment. Record 4 was taken two minutes after the beginning of the injection of pentothal and Record 5 at the close. Number 6 was taken one minute later and 7 and 8, two and two and a half minutes, respectively, after the end of the administration. Number 9, three; 10, four; 11, six; and 12, fourteen minutes after the injection. Duration of anesthesia which was difficult to determine because of the morphine was approximately one hour. P-R interval: Normal 3/25 sec.; after morphine sulphate 4/25 sec.; and after pentothal sodium 1/10 sec. Alternate normal and premature contractions are noted near the end of Record 5 at x, and can be seen in Records 6, 7, 8, and 9 at x. T-wave becomes inverted after the injection of pentothal sodium. Cardiac rates are: normal at 100; after morphine sulphate 60; and after pentothal sodium 190 beats per minute.

and Smith¹² report 31 babies as being blue and 9 pallid in their series of 500 cases with the use of nembutal (pentobarbital) and scopolamine as the anesthetic in delivering the mothers. With the use of dial in 143 obstetric cases, Bernberg and Livingston⁸ noted 8 infants lightly, 8 moderately, and 15 markedly narcotized, a total of 31 cases or 21 per cent of the babies born in their series.

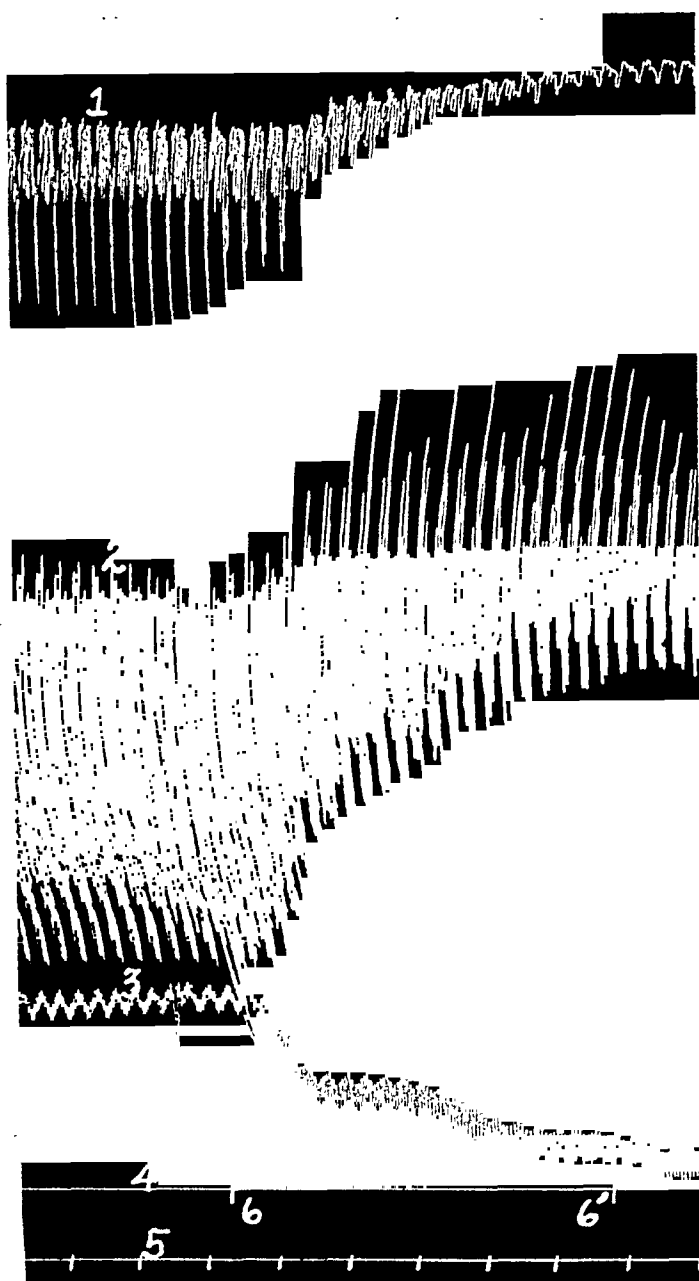


Fig. 3.—Dog, 29 kg. Ether anesthesia. 1, Auricular contractions. 2, Ventricular contractions recorded with a Cushny myocardiograph. 3, Blood pressure taken from carotid artery with mercury manometer. Heparin used as anticoagulant. 4, Point of injection. 5, Time in intervals of ten seconds and zero blood pressure. Between 6 and 6', 580 mg. sodium pentobarbital were injected intravenously.

The second source of danger is the effect on the cardiovascular system. Many investigators totally ignore this fact. It should be pointed out that all of these drugs depress the heart muscle. In experimental animals the heart dilates and the contractions become weaker as shown by

with therapeutic doses in individuals who are hypersensitive to these drugs. Leucocytosis was recorded by Warner²⁹ following sodium amytal injection in rats.

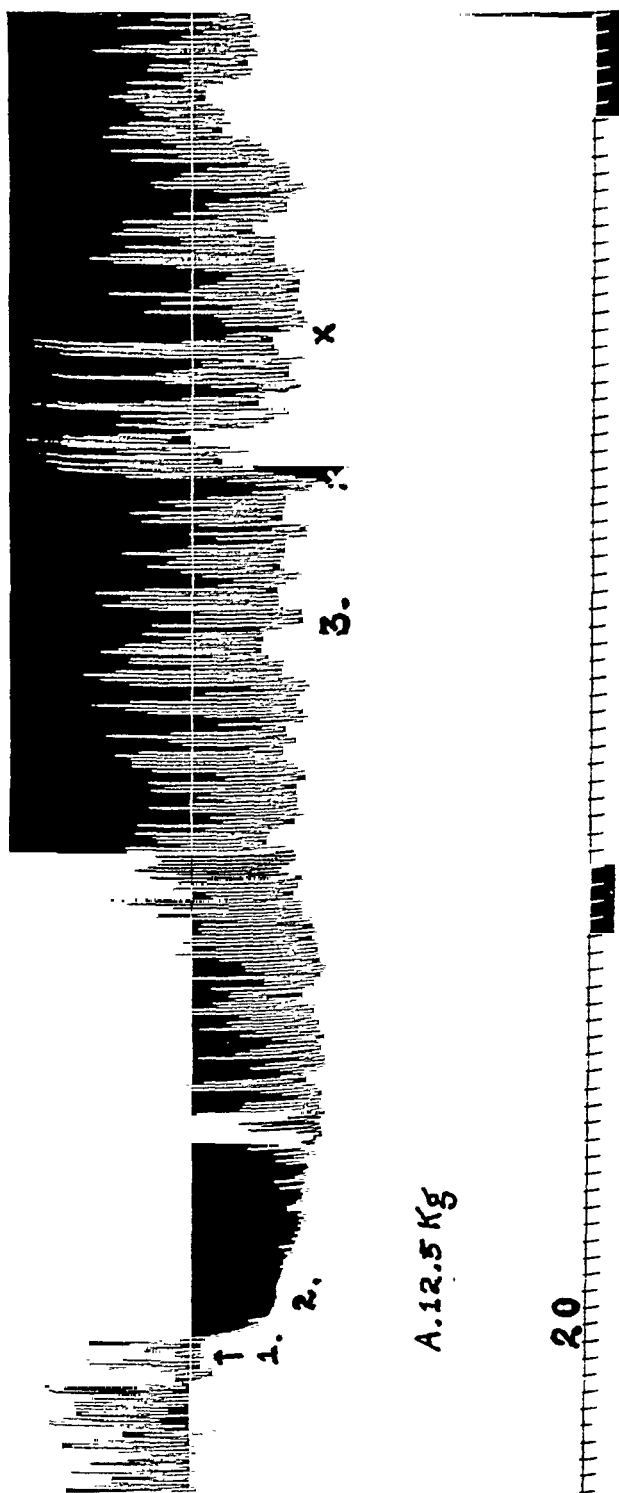


Fig. 5.—Dog weighing 12.5 kg. with Thirty-Vella loop of the jejunum. Balloon method used in recording the contractions and the changes in general tonus of the gut. The balloon measured 20 mm. in diameter and 50 mm. in length. The internal pressure was 15 cm. of water. Top record, the muscular contractions of the gut and the bottom record, the time in intervals of twenty seconds. Between 1 and 2, 300 mg. of sodium amytal were injected intravenously. Disappearance of rhythmic contractions as well as decreased general tonus can be noted. At 3 the animal woke up and at x and again at x' the animal became very excited.

The changes in the blood pressure in human subjects are very variable. All authors who have used these drugs in obstetrics report some increases and some decreases in blood pressure. Apparently the extreme drop does

the vagus in dogs and cats under amytal,²⁵ pentobarbital,²⁶ ortal and evipal²⁷ anesthesia. The increase in the maternal and fetal heart rates in obstetric cases may be due in part to such an effect. The thioderivatives, however, increase the responsiveness of the heart to the vagus stimulation. Vagus excitation with the same strength of current following thiopentobarbital, thio-ethamyl, and pentothal administration produces greater inhibition of the heart, and in some cases the slowing of the heart is changed to complete stoppage following such excitation.²⁷ It should also be pointed out that the thioderivatives cause increased irritability of the cardiac muscle itself. In dogs the average cardiac rate increases from 82 to 210 beats per minute. Electrocardiographic studies also show alternate ventricular premature contractions (see Fig. 4) and occasionally periods of paroxysmal ventricular tachycardia. Such cardiac irregularities occurred in all of the experiments performed on dogs, cats, and rabbits. In monkeys, these changes were noted only following a previous injection of 5 mg. per kg. of morphine sulphate. Morphine sulphate seems to increase the toxic effects of the thiobarbiturates.

The rate of conduction of impulses over the bundle of His is also increased. In dogs the normal P-R interval is about $\frac{3}{25}$ second. Following the injection of pentothal and other thioderivatives this time is decreased to about $\frac{2}{25}$ second (Fig. 4). An occasional premature ventricular contraction was observed in one of the dogs after three injections of evipal, but the above irregularity was never observed with the other barbiturates. Inasmuch as these cardiac findings were never recorded with the use of sodium pentobarbital, we must assume that the change in cardiac activity must be due to the sulphur in the thiobarbiturate. The thioderivatives appear to be, therefore, more dangerous than the ordinary barbiturates.

The third source of danger is that the rapid injection of any of the barbiturates causes a sudden fall in blood pressure (see Figs. 1 and 2). This fall is mainly due to cardiac injury and dilatation of the arterioles, capillaries, and venules of all the organs of the body.¹⁷ Evipal and the thioderivatives are less prone to cause marked falls in blood pressure in dogs, especially on repeated injections. This difference no doubt is due to the increased volume output by the organ as a result of the cardiac acceleration. With the thioderivatives some of our animals showed an increase in cardiac rate of over 150 beats per minute with a concomitant increase in blood pressure.

The change in the vascular bed is also reflected in the lungs. Acute edema of the lungs may result and upon the recovery of the animal bronchopneumonia²⁸ may occur. In human beings as little as 3 gr. of nembutal may produce this effect. Skin rashes and changes in the mucous membranes of the mouth may also be noted, with toxic doses, or

amytal. This is true only in excised segments. In the living animal, sodium amytal produces not only a greater decrease in the general tonus, but also a more prolonged decrease in both the force of the contractions and general tonus. The thiobarbiturates, especially pentothal and thio-

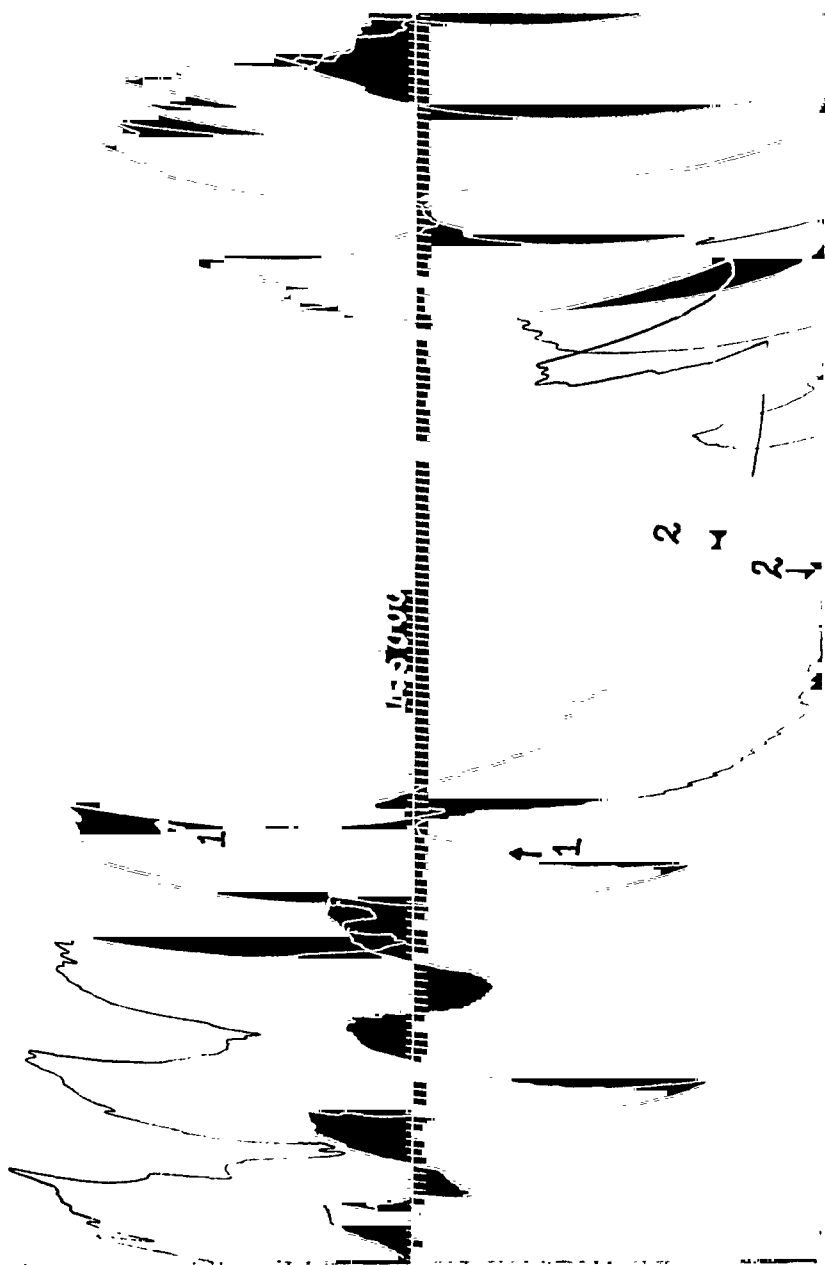


Fig. 7.—Longitudinal segments of excised rabbit uterus immersed in Locke's solution. The solution had a pH of 7.6, was kept at 38° C., and was oxygenated by bubbling oxygen through it. At 1, sodium evipal was added to the solution, making a 1:5000 dilution. At 2, the evipal solution was drained and replaced by fresh Locke's solution. As a result of the drug marked loss of tonus and disappearance of the rhythmic contractions can be seen.

pentobarbital, cause a temporary increase in tonus and with high concentrations this is followed by marked loss of tonus and complete disappearance of the rhythmical contractions. From these findings it would appear that postdelivery gas pains may not only be accentuated when present but they may even be initiated by these drugs. Loss of general tonus is also noted in the ureter and urinary bladder. This no doubt would necessitate more frequent catheterization in women following

not exceed 30 mm. of mercury.³⁰ However, it should be borne in mind that Galloway and Smith¹² report two cases of shock in their series.

The fourth source of danger lies in their depressant action on all smooth muscles, especially when large doses are given. We were able to study the effects of intravenous injection of these drugs in nonanesthetized dogs with Thiry-Vella loops of intestine.³¹ In these animals invariably the ileum, jejunum, and duodenum relaxed following the intravenous injection of doses less than the anesthetic dose of the sodium barbiturates. Not only did the general tonus of the gut decrease but also the peristaltic contractions immediately ceased and the spontaneous

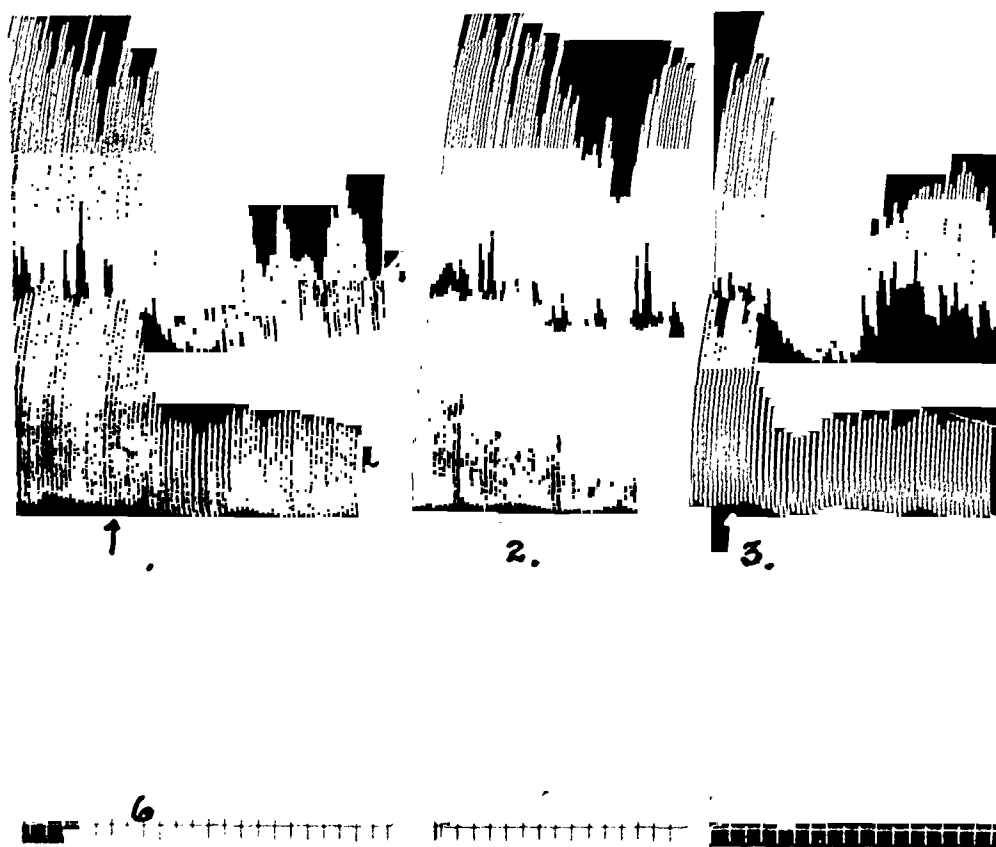


Fig. 6.—Excised longitudinal segments of rabbit intestine bathed in Tyrode-Locke's solution (equal parts) having a pH of 7.6. The solution was kept warm, 38° C. and oxygenated by bubbling air through it. The time is in intervals of twenty seconds. 4, Duodenal segment. 5, Ileal segment. 1 and 3, the effect of ortal sodium, 1:25000 solution with a pH 8.2. 2, Effect of amytal sodium, 1:25000 solution with a pH 8.6.

rhythmic contractions diminished in force and ultimately disappeared completely (see Fig. 5). We also studied the effects of these drugs on excised segments of rabbit and cat intestine bathed with warm oxygenated Tyrode's solution³² (see Fig. 6). In all cases if the pH of the bath is controlled, the true barbiturates when added to the bath invariably cause decreased tonus and with it a decrease in the force of the rhythmic contractions. A comparison of the results in Fig. 6 would seem to indicate that ortal sodium is more depressant than sodium

to the unborn fetus. I feel that they should be given either by a competent anesthetist or used only as hypnotic drugs.

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DISCUSSION

DR. HENRY S. RUTH.—I am under the impression that the gradation of psychic response and the reaction to pain is a most difficult one to evaluate by animal experimentation. Gruber's findings of cardiac irregularities developing with pentothal sodium I am sure are quite interesting to all of us who have been administering this drug and have found it quite satisfactory for a few various situations. I would like to ask Gruber if he has observed any likelihood that this response is possibly a reaction confined to the class of animals with which he has worked, in view of the fact that such irregularities have not, to my knowledge, been reported in the literature as having occurred in human beings. Lundy has reported 2,440 administrations in a twenty-month interval ending June of this year and makes no mention of such irregularities. I have been employing it somewhat during the past year and have observed a slight acceleration of the pulse rate but no arrhythmias. The fact that urologists at one large institution favor this anes-

delivery. I was unable to find statistics to support either inference upon critical analysis of the clinical reports.

The effects of these drugs upon the human uterus appear to be variable. Some writers claim no delay in delivery others report complete cessation of the contractions of the uterus for two hours.²¹ The intact and excised guinea pig uteri were studied by Drabkin and others.³³ Amytal anesthesia, they claim, does not abolish the rhythmical contractions nor does it decrease the oxytocic action of pituitary extract. In most of our experiments, we used excised segments of cat and rabbit uteri in a bath of warm oxygenated Locke's solution. The addition of any of the barbiturates or thiobarbiturates to it caused immediate loss of general tonus and decreased rhythmical contractions (Fig. 7). This depressant action varied with the different barbiturates. Generally speaking, the degree and duration of action were greater with the longer acting than with the shorter acting barbiturates. Thus, it was found in order to produce the same degree of depression a much more concentrated solution was needed of sodium evipal than of sodium pentobarbital, etc. We noted marked reduction in tonus of the intact uterus and vagina in dogs anesthetized with these drugs. Morehead and Mussy³⁴ report marked relaxation of the cervix and perineal muscles following the oral use of sodium amytal in human beings. Their findings have been confirmed by Ruth and Paxson.⁹ Bohler,¹⁰ using pernocton, reports 10 cases in which a decrease in uterine contraction existed following the expulsion of the fetus and placenta. A slowed contraction of the uterus in 4 per cent of his cases was reported by Boylan¹³ with the use of sodium pentobarbital. Levy-Solal and Sureau²¹ have shown with the use of evipal that the decreased tonus and contraction of the human uterus is directly proportional to the depth of anesthesia. In 6 of their 46 cases under profound narcosis, the forceps had to be used. They also point out the fact that the second injection of evipal caused greater depression of the uterus than did the first. This is in keeping with our findings on the anesthetic action of this drug. The duration of anesthesia is increased with each injection of the anesthetic dose in dogs. These findings, we believe, might be one of the causes for the frequent need to use the obstetric forceps in the delivery of these patients. Some obstetricians, according to their writings, used the obstetric forceps in about one-half of their cases. Galloway and Smith,¹² using nembutal and scopolamine, report only 4 spontaneous deliveries in 275 primiparous and 119 spontaneous deliveries in 227 multiparous cases. They also report increased bleeding in 20 cases. Averett,²² using the same anesthetic agents, reports 25 spontaneous deliveries and the use of the forceps in 131 cases in his series. Le Lorier and Mayer³⁵ noted severe hemorrhages after delivery in 3 of the 26 patients in whom evipan was employed.

There appears to be no delay in the delivery of the child with the use of these anesthetic agents. It may be that the restlessness and the spontaneous contractions of the striated muscles of the abdomen may hasten the complete dilatation of the cervix and soft parts of the birth canal which are already in a relaxed state due to the action of the drug.

CONCLUSIONS

In selected cases, and if given properly, the barbiturates may be fairly safe. In the hands of many, if they are used as anesthetics in unselected cases, they will be found to be dangerous drugs both to the mother and

class of drugs under consideration. If immediately below this curve of metabolism we draw the four stages of anesthesia, the practical application will become more apparent. The first stage of anesthesia is the stage of analgesia, the upper portion of which consists of relative analgesia which increases in intensity as the lower border of the stage is reached, until at the very lowest border a narrow margin of total analgesia is obtained just before entering the second stage. The second stage is the stage of delirium. Below this, of course, appears the third or surgical stage with its four strata and finally, the fourth stage. With both of these latter two, however, we are not concerned at this time.

By the use of drugs producing analgesia we can enter the first stage, and, if we are fortunate, place the patient in total analgesia. I should like to repeat, however, that the barbiturates are essentially hypnotic and are but mildly analgesic. When the dosage is increased beyond certain limits in an effort to reach total analgesia, the patient will be thrown into the stage of delirium, and restlessness results. Because the barbiturates are more amnesic than analgesic in action, it is better to be satisfied with a loss of memory of the pain alone by their use, for we will repeat, when sufficient dosage has been prescribed to prevent pain perception, the vital reflexes are dangerously depressed. If, in a situation of such depression an inhalation anesthetic is superimposed, in order to keep the patient quiet for the actual delivery, a fatality may easily be encountered if the anesthetist is not aware of both the presence and the dangers of this depression.

DR. J. O. ARNOLD.—We have failed to be convinced, through the years since the barbiturates have been in vogue, that their use could be as successfully or as satisfactorily practiced in the homes as in the hospitals. Therefore, after trying out one after another of these newer combinations, we have practically dropped them all, and gone back to older, more reliable and less troublesome methods. Many years before the outbreak of the "twilight sleep" epidemic we had been using morphia and scopolamine, and when that procedure had been pushed to the extreme by the popular press, we swung over to the morphia and magnesium sulphate combination, after the technic of Gwathmey. Then came the barbiturates, but now for about three years we have given these up also, and gone back once more to a modified Gwathmey course, dropping the magnesium sulphate, and giving the plain morphia, followed more or less closely by "E.O.Q."—ether, oil, and quinine, by bowel. We are convinced that our present results are as good as with any other method we have pursued, and much less complicated and troublesome to apply.

The effects on the mothers, mentally and physically, are certainly no less satisfactory than those produced by the barbiturates. The supervising maternity nurse, who has been on the service for many years and has observed all these varying procedures in the hands of many different doctors, is unqualified in her endorsement of our present methods. A review of our records for the past three years shows also a steadily lowering infant mortality, which would hardly be the case if we had many narcotized babies.

I am quite sure that if we follow these old-fashioned methods with as much attention and care in their clinical application as is being devoted to the safeguarding of the barbiturate victims, we shall get better all-around results. Furthermore, we will have something to teach our students that will not only be safer, but that will undoubtedly be more generally applicable under the conditions in which most of their work will be done, where special nurses and sideboarded beds, and all that sort of expensive equipment can seldom be provided.

DR. PHILIP WILLIAMS.—During the past few years those of us who have attended the monthly reviews on Maternal Mortality at the Philadelphia County Medical Society realize that there have been a number of cases, possibly 18 or 20,

thetic above all other anesthetic agents and methods for their endoscopic trans-urethral resections, which, of course, are usually indicated in old men, speaks for the possibility that their action on the cardiovascular system is a rather insignificant one.

It does not seem probable that these *shortest* acting barbiturates (evipal and pentothal sodium) with their analgesic properties will play a major part in the pain control in normal obstetrics, for in these affairs we desire and require longer action. We, therefore, should perhaps be more in order in this discussion by confining our remarks to the *shorter* acting barbiturates of the class of sodium amytal, pentobarbital sodium, etc. Their pharmacologic action is similar when considered as a class. They are depressing to metabolism. It should be remembered that they are essentially soporifics, acting primarily on the intellectual centers, and have but very slight analgesic action. When sufficient dosage has been prescribed to prevent pain perception, the vital reflexes are dangerously depressed. The amounts required of them to produce a given therapeutic effect in their clinical application bear approximately the same relationship to the minimum lethal dose; for example, pentobarbital sodium is twice as toxic as sodium amytal but only one-half as much is required to produce comparative effects. When too large dosages incur complications, the shorter acting barbiturates are fatal through respiratory depression and the longer acting ones through pulmonary complications, edema, and pneumonia. Idiosyncrasies are perhaps no more common than occur with morphine and should be combated by oxygen therapy, and coramine intravenously or intramuscularly, metrazol subcutaneously or intravenously, or perhaps by picrotoxin. Whereas it is true that these drugs depress the involuntary musculature, it has been shown by many investigators that the resistance of the uterine muscle fibers in situ is quite high.

I believe that a little plan employed by many of us to determine the dosage of preanesthetic sedatives might prove of value to select the dosage of the barbiturates for various individuals. By this plan we take cognizance of the fact that to obtain beneficial effective preanesthetic sedation several factors must be considered.

It has been shown, especially by Guedel, that the curve of reflex nerve irritability parallels the curve of metabolism; cell oxygen demands, of course, parallel metabolism. The amount of an anesthetic agent to provide a given depth of anesthesia will increase or decrease in a direct ratio with an increase or decrease of metabolism. Therefore, a curve over the required amount of anesthesia parallels closely the curve of metabolism. We desire normal metabolism in order to decrease the amount of anesthesia. Therefore, an estimation of the factors which cause a deviation in the basal metabolic rate will yield indispensable evidence which will serve as an aid for the correct dosage for each individual.

One of the most important factors, because of its consistent application, is the effect of age upon the metabolic curve; but because this is of small relative importance in obstetrics, the normal metabolic curve for various ages will merely be drawn upon the blackboard without further elaboration. Another factor is that of temperature; for each degree of fever there is a 7 per cent increase in metabolism. Emotional activity, such as fear, apprehension and anger will exert a profound influence usually in the upward direction, but this can only be estimated and not measured. Pain exerts a substantial effect in direct ratio to its severity. Specific toxemias, of which thyrotoxicosis and neurosyphilis are notable, raise reflex nerve irritability and therefore resistance to hypnotic sedation. Drug addicts and alcoholics also show a resistance. The body weight of the individual is of some importance when the excess weight is not due to fat; the factor of sthenicity is of greater importance. We shall illustrate on this metabolic curve on the board the effect of some of these factors, and how they will influence the dosage of the

When I first started to use nembutal and scopolamine, I used it in a dosage of 4.5 gr.; but for the last eight or nine months I have been giving almost routinely 9 gr. nembutal and 1/150 scopolamine as an initial dose, and giving it as early as possible. In other words, as soon as I was certain that the patient was in labor, irrespective of the amount of dilatation or effacement. Giving these drugs early in labor unquestionably gave better results. The amount of excitement in the individual patient has been markedly decreased by giving a larger dose of the drug, and we have also found that in the occasional patients who become wildly excited, the addition of rectal ether will quiet them down, particularly if the rectal ether is given while the patient is under light nitrous oxide anesthesia.

In conclusion, I realize that we are dealing here with drugs that, if used promiscuously and in private homes or in poorly equipped institutions, might increase the dangers to both mother and child, but I feel very strongly that any woman, no matter from what stratum of society, is entitled to the relief of the pains of childbirth, if it can be done with safety to both her and her unborn child. Until some different method is evolved, or until I see some of the dangers which are now attributed to these drugs, I shall continue to endorse their use and continue to use them.

DR. EDWARD SCHUMANN.—I wish to call your attention to three or four points.

The first is that only within the last few years have women demanded amnesia in labor. From the time of Simpson and before, relief of pain was sought. Now this has suddenly become secondary, and it is of exceeding importance that the woman does not remember that she has been in labor. That has been bolstered, mainly, by current literature and lay magazines.

The second point is, and I think all of us will agree, that the more profound the analgesia the greater the inhibition of normal mechanism of labor, and therefore since it is in the minds of some of us to return to a greater degree of normalcy in the conduct of obstetrics and to secure, if possible, the highest percentage of spontaneous deliveries, we must lessen the degree of analgesia which we present to our patients.

The third point is the fact that we have got to a point, where we are controlled by our patients with regard to analgesia, and I consider this grave from the standpoint of the medical profession. The patient demands painless labor. I believe, as a group we should confront the patient with the statement that we choose the analgesia and conduct the labor to her best interests.

Banerji, Kaligati: A Study of Maternal Mortality and Morbidity in Bengal, J. Indian M. A. 5: 607, 1936.

The author deplors the prevailing poor conditions in Bengal. The maternal mortality rate is high. Per 1,000 births in India, there is a mortality of 16.6 in Madras City and of 42 in Tea Gardens in Assam.

Bengal requires a well-planned organization and a good scheme of cooperation to institute proper maternal care, both prenatally and intrapartum. The midwives (dais), as they exist at present, are inefficient, untrained, incapable and a source of sepsis to the parturient.

The hospital should have an antenatal clinic under a trained doctor and midwives. The mothers need to be advised as to proper food and living during pregnancy, labor, and the puerperium. They must be taught to report to the thana clinic if abnormalities occur. A strict program of public health must be initiated if the gross mortality and morbidity are to be reduced.

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in which the administration of the barbiturates during the labor has had a certain degree of influence toward the fatal outcome of these cases.

In some instances, no other factors could be elicited and the death was undoubtedly due to some action of the sedative. In others, the depression caused by the drug placed the patient in jeopardy when inhalation anesthesia and operative procedures of various types were added to the burden already carried. In the remaining cases, the drugs used may or may not have played a part in the death.

As has been expressed many times the most important requirement of a sedative agent lies in the safety of its use. We cannot grant that the barbiturates are perfectly safe to use in all labors. The idiosyncrasy of the patient to the drug must be taken into account. In not less than three cases, an idiosyncrasy was manifested by the development of cyanosis, respiratory embarrassment, and edema of the lungs with increasing shock from which the patients did not recover.

The susceptibility of a patient to the barbiturates or a patient's tolerance to the barbiturates form questions as yet unsolved. The prolonged coma in which some parturient women remain after the average or ordinary dose of such sedation proves without doubt that occasionally some individuals possess a high susceptibility to the action of these agents, while others are unusually tolerant and may require much more than the average dose before sedation is produced. In a number of the patients where labor had ceased with the patient in the peculiar deep coma following exhibition of barbiturates, ether anesthesia and major procedures were followed at times by uncontrollable postpartum hemorrhage, at other times by shock and collapse which resisted the usual measures of treatment.

In the remaining cases, while the barbiturates may or may not have played a part in the fatal outcome, it was evident to those who heard the discussion of such cases that the barbituric acid derivatives formed a dangerous background to an operative delivery.

I feel that the element of safety in the use of these drugs has not been entirely proved, and a considerable degree of caution, especially as to the dosage, must be exercised before they are exhibited in the patient who may require major obstetric procedure for delivery.

DR. CLIFFORD B. LULL.—I cannot agree with the things that have been said, as the use of this group of drugs in the practice of obstetrics has slowly but surely raised my enthusiasm for them. The important thing to remember is when and how to use these drugs in obstetric work, and I believe that if nembutal and scopolamine are used properly, the danger arising will be minimized.

In experience extending over approximately three and a half years, and in about 4,000 cases, I have not seen the serious complications that I have seen without the use of analgesia, or with the use of other analgesic remedies. As far as increasing my operative percentage of deliveries, it has not done so, because my operative deliveries in private cases have been almost 100 per cent. I believe the mistake is being made by classifying outlet forceps, that is, when the head is crowning, as an operative procedure. I admit, with the use of these drugs, that this is usually essential because the patients are restless with the pains, and if they are not delivered under light nitrous oxide anesthesia, the operative field might be contaminated. I am convinced, however, that by the use of these drugs, the more difficult forceps operations and the incidence of version have been very decidedly decreased. I have not seen postpartum hemorrhage, neither have I seen narcotized children. Further, I am convinced that the duration of labor, particularly in nulliparous individuals, is decidedly shortened, and I am certain that the cervical traumatism have been very markedly decreased.

The committee is of the opinion that "frequent and injudicious employment of deep analgesia and anesthesia has increased very materially the rate of operative interference, and has on this account been a major factor in preventing a reduction in the high maternal mortality rate in this country."

Before condemning these assertions as reactionary, let us turn to the results of maternal welfare study in Philadelphia and ascertain how we are progressing with the management of labor and how our results are influenced by deep obstetric analgesia and anesthesia.

While the general maternal mortality rate in Philadelphia has decreased 24 per cent from 1931 to 1935, this decrease is accounted for solely on the basis of a 49 per cent decline in nonpreventable deaths. The preventable death rate has remained uniform throughout the five years. While the death rate per 10,000 live-births, which is attributable to errors in judgment and technic on the part of the physician, has decreased 9.5 per cent, yet the proportion of maternal deaths due to these errors has increased 11 per cent.

If one considers the maternal deaths during or within twenty-four hours after labor, the rate of preventable deaths and the share in responsibility of the physician for them rises amazingly. In this group there is no change in the maternal death rate for the five-year period. The nonpreventable death rate has decreased 49.3 per cent; the preventable rate has risen 52.5 per cent. The death rate from errors in judgment and technic on the part of the physician as manifested in sudden deaths at delivery has jumped 108.5 per cent, and the proportion of maternal deaths due to these errors has increased 107.3 per cent.

When these statistics are assembled, one may conclude that here is the explanation of our failure to progress. A consideration of the death rate from all other conditions of childbearing confirms this opinion. In this group there is a decrease in the maternal death rate of 28.9 per cent, in the nonpreventable death rate of 48.6 per cent, in the preventable rate of 11.1 per cent, in the death rate from errors of judgment and of technic on the part of the physician of 41.4 per cent, and in the proportion of deaths due to these errors of 5.5 per cent.

A general reduction of mortality in all its phases then in 876 of 1,096 cases, but no reduction in mortality in the remaining 220! An improvement in all phases of obstetric practice except those which have to do with labor, and in the latter an increase of over 100 per cent in the responsibility of the physician for sudden death! End-result, no change for five years in the preventable maternal death rate; instead, a general increase of 11.1 per cent in the proportion of maternal deaths due to errors in judgment and technic on the part of the physician!

Evidently something is wrong with our methods of management in labor, and saddest to relate, whatever is wrong is going "more wrong" in every succeeding year.

ANALGESIA WITH THE BARBITURIC ACID DERIVATIVES AND ITS RELATIONSHIP TO SUDDEN DEATH IN LABOR*

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NO TOPIC in obstetric procedure is more provocative of discussion than that of analgesia and anesthesia. Journals are filled with reports of assorted methods and new combinations, and every patient who comes to register wants first to know what will be done to eliminate the pangs of labor. She wishes to go to sleep with the first pain and wake with the baby in her arms, and she is sure from her reading that this is not only feasible but it is her rightful privilege.

Particularly has this been true since the introduction of the barbituric acid derivatives. Immature intimations as to the success of these products have been avidly seized upon by the public. Certain women's magazines make of each new obstetric analgesia their protégé, announce it as the panacea for women's suffering and the remedy without which any physician who assays to practice medicine is a nonentity or a Rip Van Winkle. Thus the manner of sensationalizing which started thirty years ago in the far-flung propaganda for "twilight sleep," and which repeated itself in the case of Gwathmey anesthesia and pernocton, is now busied with the newer forms, amytal and nembutal.

Just as occurred with each of the previous methods, the time comes to weigh carefully in the balance the safety and the therapeutic effectiveness of these agents.

From various sources, doubt has arisen as to the effect which deep analgesia and anesthesia have upon the intelligent and safe conduct of labor. In its much criticized report on "Maternal Mortality in New York City," the Committee on Public Health Relations of the New York Academy of Medicine state the following in reference to this question:

"The use of anesthesia during labor and delivery has grown steadily in extent since its introduction in the last century, and is a problem of the most pressing importance, more so in the United States than in any country. This has come about to a large extent through pressure from the lay public. The women of the large urban centers have become steadily more insistent in their demands for shorter and less painful parturition, and the accoucheur may disregard these demands only at great risk to his own practice."

*Presented at a meeting of the Obstetrical Society of Philadelphia, November 5, 1936.

Their action in the former direction is greatly enhanced by the addition of scopolamine. The patient may scream as if in great agony during the course of her labor pains, but wake the morning after with no clear recollection of what has taken place. In his analysis of obstetric analgesias, Irving states that he considers no method successful which gives less than 100 per cent amnesia. The factor of relief from pain he considers a minor consideration.

The advocates of the method claim that their drug supplants morphine, having none of its disadvantages and many advantages. They state that it does not delay labor, does not narcotize the baby, and that it makes the patient forget the unpleasant experience of childbearing. Several maintain that morphine has no further place in obstetric practice because of its ill effect on fetal respiration.

A great disadvantage of the barbiturates is the restlessness they produce. Patients under their influence may prove difficult to control. In such a confused and semistuporous state of mind, pain arising from the uterine contraction is misinterpreted, and the parturient becomes uncontrollable. As the time for actual delivery approaches, the confusion increases. Careful surgical preparation and spontaneous delivery under such circumstances are impossible. Usually the patient must be anesthetized with gas or ether and delivery consummated by low or mid-forceps. The labor over and the pains dispatched, the patient falls into a deep slumber and remains almost comatose for a number of hours.

The most enthusiastic users of the nembutal scopolamine technic acknowledge that the rate of operative interference is thereby multiplied many times, that forceps delivery becomes essential in from 40 to 60 per cent of cases. They also emphasize that patients under the influence of nembutal must be watched with the closest attention, their care individualized, and precautions taken that no injuries occur during the

TABLE I. HOW IS THE MEDICAL PROFESSION FULFILLING ITS RESPONSIBILITIES IN THE VARIOUS GROUPS OF MATERNAL DEATHS? 1931 VS. 1935

	ALL MATERNAL DEATHS	MATERNAL DEATHS DURING OR 24 HR. AFTER DELIVERY	ALL OTHER MATERNAL DEATHS
Maternal death rate	Decrease of 24%	No change	Decrease of 28.9%
Nonpreventable death rate	Decrease of 48.9%	Decrease of 49.3%	Decrease of 48.6%
Preventable death rate	No change (1%)	Increase of 52%	Decrease of 11.1%
Death rate from errors in judgment and technic on part of physician	Decrease of 9.5%	Increase of 108.5%	Decrease of 41.4%
Proportion of deaths due to errors in judgment and technic on part of physi- cian	Increase of 11.1%	Increase of 107.3%	Decrease of 5.5%

Probably there are a number of points that are amiss in the conduct of labor, and doubtless it is a mistake to attribute these disturbing trends to faults in obstetric analgesia and anesthesia. Nevertheless, when one analyzes the methods used in the fatal cases and the part that the methods played in fatality, this consideration assumes a major importance.

The records reveal that in six of eleven instances in which nembutal was used, death was attributable to the analgesia, quite evidently in two, quite probably in the other four. In two additional instances the choice of the analgesic method, in view of the patients' condition, seemed singularly bad. In the eight instances of amytal administration there were two in which the analgesia was quite possibly the cause of death and two in which the selection of the method seemed injudicious.

While it is most difficult to say certainly that the analgesic method was responsible for the fatality, yet the evidence is preponderantly in that direction. The suspected cases had these points in common: there was no other factor of enough significance to account for fatality; all the patients succumbed with a peculiar type of cyanosis and respiratory depression, rapid thready pulse, and shock without hemorrhage which failed to react to the usual methods of treatment. In several instances the deaths were ascribed to heart failure or to pulmonary embolism. If this were the true diagnosis, it is peculiar that so many instances should have occurred in the barbituric acid group. Of the frequently made diagnosis "pulmonary embolism" Kerr says: "There is little doubt that a considerable number of deaths are attributed to pulmonary embolism which should really be relegated to trauma or shock or both. The diagnosis of embolus is a simple explanation and salves the conscience of the person in attendance."

The barbiturates are presumed to have a fairly wide margin of therapeutic safety. This is said to be the case particularly of sodium pentobarbital, or nembutal (Sollman). The reports of Irving,⁸ Galloway,⁵ and Daichman⁴ reveal no maternal anesthetic death. There seems, however, to be a wide range of susceptibility to the action of the drug. For instance Galloway describes one case in which 22 gr. of nembutal were administered in the course of labor without any apparent effect, and the patient at the conclusion stated that she thought she had had a very hard time. On the other hand, Willeox, in the *British Medical Journal* of 1934 (1:417-418), emphasizes the importance of peculiar susceptibility to the drug and states that he has seen a number of cases in which sudden collapse, respiratory depression, and death from bronchopneumonia occurred, where only 3 gr. were administered. He particularly opposes the use of the drug as a preparatory or basal anesthetic.

For their effectiveness in labor the barbiturates depend upon ability to produce forgetfulness (amnesia) and very little upon analgesia.

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EFFECTS UPON UTERINE MOTILITY OF URINE FROM DYSMENORRHEIC AND NORMAL INDIVIDUALS*

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THE present investigation was undertaken in an effort to gain some information concerning the factors underlying essential dysmenorrhea. In spite of the importance of this disorder, comparatively little experimental work on its cause and essential features has been done. The nature of menstrual pain has led clinicians to attribute it to spasmodic or exaggerated contraction of the uterus, an assumption which is supported by the fact that the spontaneous motility and the sensitivity of the human uterus are especially marked just before and during menstruation.¹ Moir,² using an intrauterine bag, obtained records of uterine contractions and intrauterine pressure in a patient with dysmenorrhea and in a normally menstruating woman. The chief point of difference was in the pressure, which reached a maximum of 150 mm. of mercury in the dysmenorrheic patient, as compared with 120 mm. in the normal woman.

To explain the underlying cause of the painful contractions, a number of theories have been advanced. They have recently been reviewed by Novak and Reynolds³ and by Israel.⁴ Those of widest application postulate abnormal variations in humoral factors influencing uterine motility. An examination of the action of blood or urine upon uterine motility seemed, therefore, a logical method of approach to the study of dysmenorrhea, especially since results reported by a number of investigators indicate that certain variations in the effects of blood or urine obtained under different physiologic and pathologic conditions can be demonstrated.⁵⁻¹⁴ Because it is readily obtainable in adequate quantities, urine was chosen for investigation in the present study. This includes a series of experiments in which tests were made of the action

*The data in this paper are taken from a thesis presented to the Graduate School of Vanderbilt University in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Anatomy. The work was done under the supervision of Dr. J. M. Wolfe, Assistant Professor of Anatomy. The experimental methods and data, which have been presented in greatly abbreviated form, will be published in full in the author's thesis, which is available in the Vanderbilt University Library.

more restless periods. For this reason the method is available for use only in the hospital; it can only be a source of grief if undertaken in the home.

TABLE II. AMNESICS, ANALGESICS, AND ANESTHETICS EMPLOYED IN THE PATIENTS WHO DIED DURING OR WITHIN 24 HOURS AFTER LABOR

AGENT USED	NUMBER OF DEATHS IN WHICH AGENT WAS EMPLOYED	PRIMARY CAUSE OF DEATH	POSSIBLE CAUSE OF DEATH	POORLY SELECTED
Ether or nitrous oxide, oxygen, ether	108	1 (1%)	1 (1%)	1 (1%)
Nitrous oxide, oxygen	34	0	1 (3%)	9 (26%)
Gwathmey	7	0	3 (43%)	1 (14%)
Chloroform	3	0	1 (33%)	2 (66%)
Spinal	4	2 (50%)	1 (25%)	1 (25%)
Local	4	0	0	0
Nembutal	11*	2 (18%)	4 (36%)	2 (18%)
Amytal	8*	0	2 (25%)	2 (25%)
None	40	0	0	0

*Possibly more. These deaths are being subjected to further study.

Considering these facts, one questions whether nembutal-scopolamine amnesia fulfills the requirement of safety. If the patient is in constant danger of injuring or contaminating herself, if her cooperation in the course of labor is utterly lost, if the incidence of operative interference is multiplied tenfold, if the supervision of the case is transformed from an intelligent conduct of labor into the treatment of drug confusion, one doubts that the effect is worth the reaction that it produces.

This method is at the height of its popularity. Reports of recent publication have been favorable, as they are always at such time. However, now that the method is getting away from the centers of its propagation and is being put into more general use, questions are arising as to efficacy, difficulty of management, and sudden death. In the crucible of general usage, the gold is separating from the sludge and that which is materially and permanently worth while is being refined.

In the light of such relentless scrutiny, it appears uncertain that deep analgesia with the barbiturates is completely safe or fully reliable. It is questionable whether the widespread acceptance of this method is a step forward in obstetric practice.

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TABLE I. DISTRIBUTION OF TYPES OF RESPONSES AND OF POSITIVE OXYTOCIC AND INHIBITORY EFFECTS, CONSIDERED SEPARATELY, IN RELATION TO THE CONDITIONS PRESENT AT THE TIME OF COLLECTION OF EACH SPECIMEN OF URINE

PHASE OF MENSTRUAL CYCLE												MEN	TOTALS
DYSMENORRHEA				MILD CRAMPS				NO CRAMPS					
No. individuals represented No. menstrual periods represented by intermenstrual specimens No. specimens investigated	Responses in which : Oxytocic phase positive; inhibitory phase positive Oxytocic phase positive; inhibitory phase absent or insignificant Oxytocic phase absent or insignificant; inhibitory phase positive Insufficient responses No demonstrable effect Positive oxytocic effects (considered separately) Positive inhibitory effects (considered separately)	MENSTRUATION SPECIMEN VOIDED DURING MOST SEVERE CRAMPS	MENSTRUATION SPECIMEN VOIDED BEFORE OR AFTER MOST SEVERE CRAMPS	INTER-MENSTRUUM	INTER-MENSTRUATION	INTER-MENSTRUUM	INTER-MENSTRUATION	MENSTRUATION	INTER-MENSTRUUM	INTER-MENSTRUATION			
11 14 15		11 14	12	9 15	7	12 19	8	37* 58*					
33.3 66.6 ---		26.3 42.1 ---	22.22 27.77 ---	45.0 10.0 15.0	40.0 10.0 23.3	35.0 10.0 35.0	36.0 12.0 8.0	50.0 12.5 25.0					
100.0 33.3		68.4 26.3	50.00 50.0	55.0 60.0	50.0 63.3	45.0 70.0	48.0 44.0	62.5 50.0					

*In some instances, the same individual or the same menstrual period is represented more than once. This is due to the fact that some women experienced different degrees of menstrual discomfort at different periods investigated and also to the fact that, in some instances, more than one urine specimen was collected at a single menstrual period.

upon uterine motility of urine obtained from women who experienced varying degrees of menstrual discomfort. Urine from men was used as controls.

METHODS

Degrees of menstrual discomfort were defined as follows: *Dysmenorrhea*, menstrual cramps of incapacitating severity. *Mild cramps*, menstrual cramps of minor severity which interfere in no way with usual activities and which are relieved by mild medication. *No cramps*, a condition in which menstruation is accompanied by no cramps, although there may be a minor degree of vague general discomfort.

Urine was obtained from 37 individuals: 10 women with dysmenorrhea, 12 women with variable menstrual symptoms, 7 women with no cramps, and 8 men. In all of the cases of dysmenorrhea, pelvic pathology as an etiologic factor could be excluded.*

Single urine specimens were obtained from men. Specimens from women were collected, as a rule, during two or more consecutive menstrual periods and at intervals of one week or less during the intermenstruum. Intermenstrual specimens were classified according to the degree of discomfort present at the following menstrual period. One hundred and seventy-three specimens of urine were investigated. Their distribution with respect to sex, to phases of the menstrual cycle, and to the degree of menstrual discomfort is shown in Table I.

By means of the uterine fistula technic developed by Reynolds,¹⁵ the urine was tested for its effect upon the motility of the uterus in situ in unanesthetized, castrate rabbits. Uterine motility was recorded on a smoked drum by means of an intrauterine balloon connected to a tambour through a water and air transmitting system. Using this technic, Reynolds showed that after castration the uterus of the rabbit becomes quiescent¹⁶ and does not respond to stimulation unless rhythmical motility has been induced by the administration of estrogen.¹⁶⁻¹⁸ For this reason, the test animals were injected with estrogen† approximately twenty-four hours previous to the injection of urine.

In testing the urine, two procedures were followed. In the first, 0.2 c.c. of pituitrin‡ was injected thirty minutes after the injection of urine. The response to pituitrin served as a control of uterine sensitivity;¹⁹ it was also useful in demonstrating certain effects of the urine. In the second procedure, which was adopted as an additional test of the effect of urine upon the response of the uterus to a subsequent injection of pituitrin, the pituitrin was injected one hour before and again ten to fifteen minutes after the injection of urine. Both urine and pituitrin were injected intravenously. The dosage of urine was not constant but was regulated by the response; this was necessary because of the toxicity of specimens voided during dysmenorrheic cramping. The maximum dose was 20 c.c. All urine specimens were tested as in Procedure 1§; 42 specimens from women, representing all of the groups shown in Table I, were also tested as in Procedure 2.

EXPERIMENTAL RESULTS

Effects of Pituitrin.—For purposes of comparison with effects obtained following the injection of urine, responses to pituitrin in animals not previously injected with urine (Procedure 2) are illustrated in Fig. 1. They were essentially similar

*The suitability for the purposes of this study of the individuals from whom urine was obtained was approved by Dr. John C. Burch, Associate Professor of Obstetrics and Gynecology.

†Theelin, Parke, Davis and Company, or Progynon B, Schering Corporation.

‡Pituitrin-S, Parke, Davis and Company.

§In a few of the earlier experiments, pituitrin was omitted after positive responses to urine.

phases were positive (Fig. 3). In 39 responses the oxytocic phase was positive, the inhibitory phase absent or insignificant in magnitude (Fig. 4). In 29 responses the oxytocic phase was absent or insignificant, the inhibitory phase positive

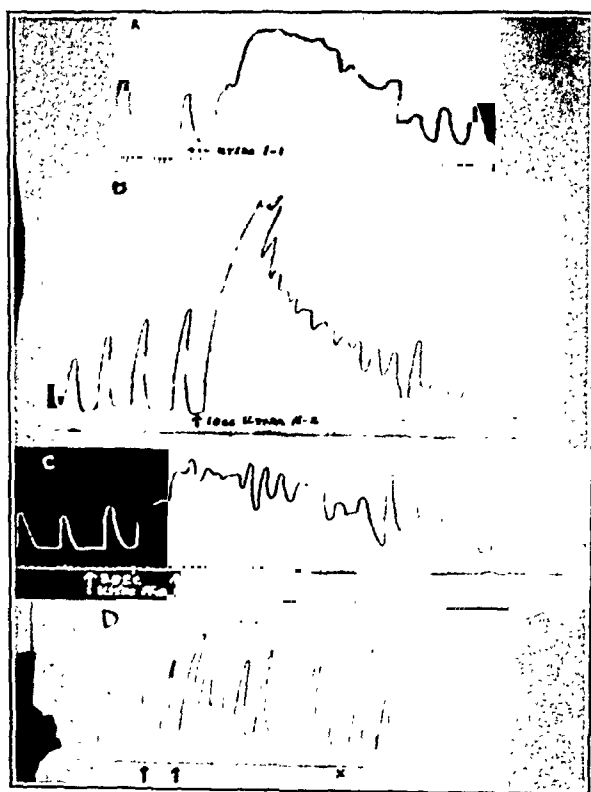


Fig. 2.—Responses to urine showing oxytocic effects. A, B, C, Positive oxytocic effects. D, Insignificant oxytocic effect.

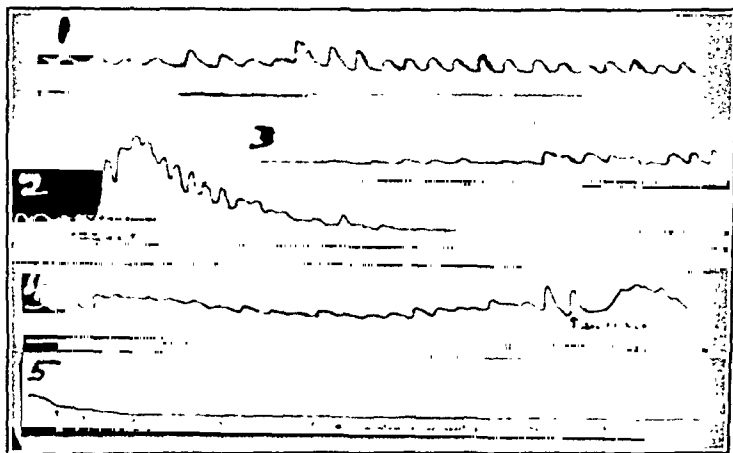


Fig. 3.—Response to urine (Tracing 2) in which both oxytocic and inhibitory phases were positive. Response to pituitrin (Tracing 4) reduced in magnitude (compare with Fig. 1, D).

(Figs. 5 and 6). In 30 responses one or both phases were present but insignificant (Fig. 2, D). Sixteen specimens of urine produced no demonstrable effect.

The responses obtained were related to the conditions present at the time of collection of each specimen of urine as shown in Table I and in Charts I and II. The table and charts also show the distribution of positive oxytocic and inhibitory effects considered separately.

to those described by Reynolds;¹⁹ i.e., an initial oxytocic effect was followed by a period in which the rhythmical motility was inhibited to a greater or less extent. Evidence of both oxytocic and inhibitory effects was present in all of the records obtained; oxytocic effects were invariably strong, but inhibitory effects were slight in about 20 per cent of the tests (Fig. 1, C). Following the response to pituitrin, the return to motility of the original type and degree was gradual; it was usually complete one hour after the injection. Responses to urine injected at this time were often reduced in magnitude, which indicates that decreased sensitivity of the uterus due to pituitrin may persist after the return of rhythmical motility.

Responses of the uterus to pituitrin in animals previously injected with urine (Procedure 1) were in every way similar to those described above, except that they were sometimes reduced in magnitude. Occasionally the initial tetanus was incomplete (Fig. 3).

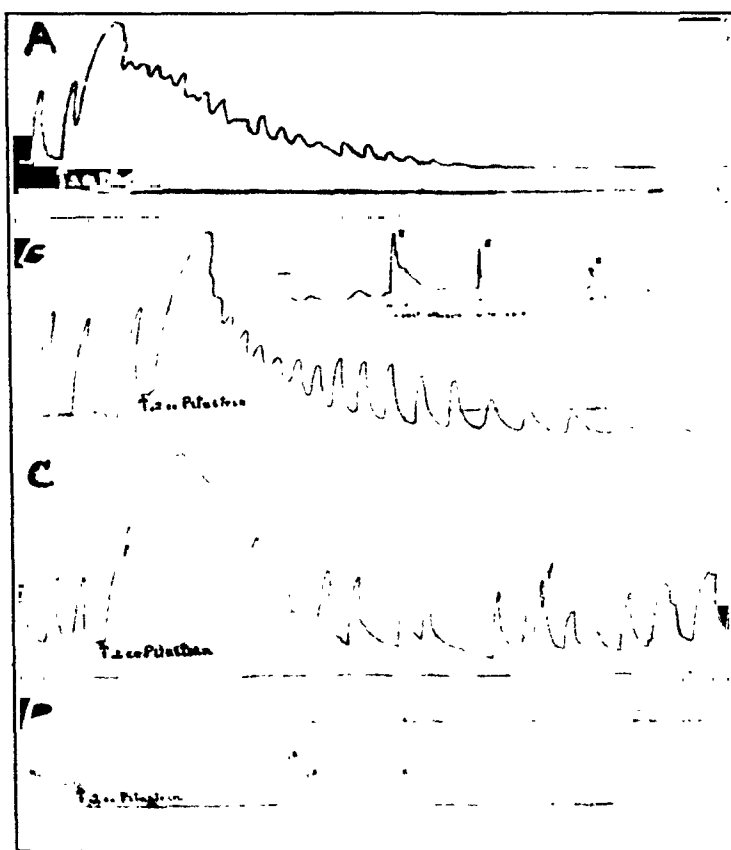


Fig. 1.—Uterine responses to pituitrin in animals not previously injected with urine. x, micturition.

Effects of Urine.—The basic response of the uterus to urine consisted of an initial phase of contraction (oxytocic phase) (Fig. 2), followed by a decrease in the degree of rhythmical motility and a reduction in the sensitivity of the uterus to pituitrin (inhibitory phase). In 60 responses, the inhibitory effect upon the rhythmical motility was indicated by a period of relative quiescence similar to that produced by pituitrin (Figs. 3 and 5). These responses were followed by gradual return of the original motility. In 28 responses, the inhibitory effect was indicated by a gradual decrease in the amplitude of the rhythmical contractions with no return to motility of the original degree (Fig. 6).

The responses produced by different specimens of urine varied in magnitude with respect to one or both phases. In 59 responses both oxytocic and inhibitory

from men and from nonmenstruating women with no cramps were of this type. Variations in the percentage of positive oxytocic or inhibitory effects in the other groups were dependent chiefly upon variations in the number of responses in which only one phase was positive. This was especially true with respect to differences referable to menstruation and to the intermenstruum, respectively, in each group of women.

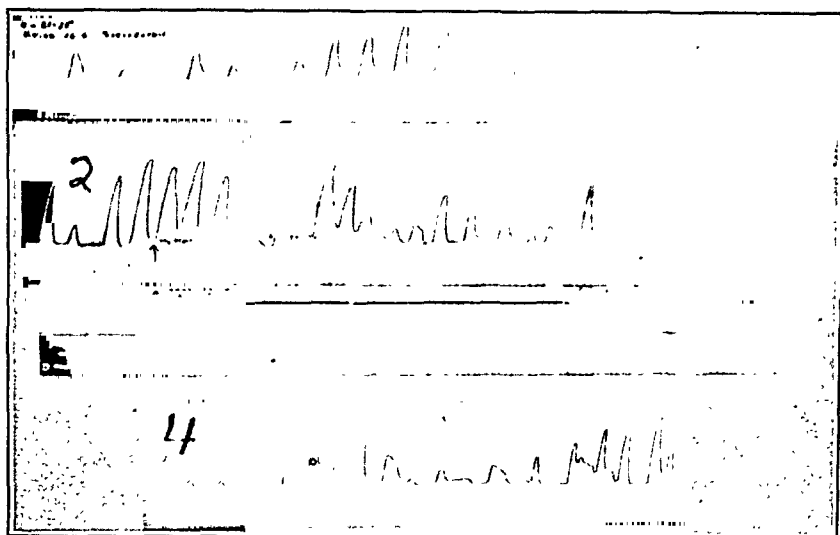


Fig. 5.—Response to urine in which the oxytocic phase was negative, the inhibitory phase positive, as indicated by complete inhibition of rhythmical motility (Tracings 2 and 3). Urine injected at arrow in Tracing 2. Return of motility in Tracing 4.

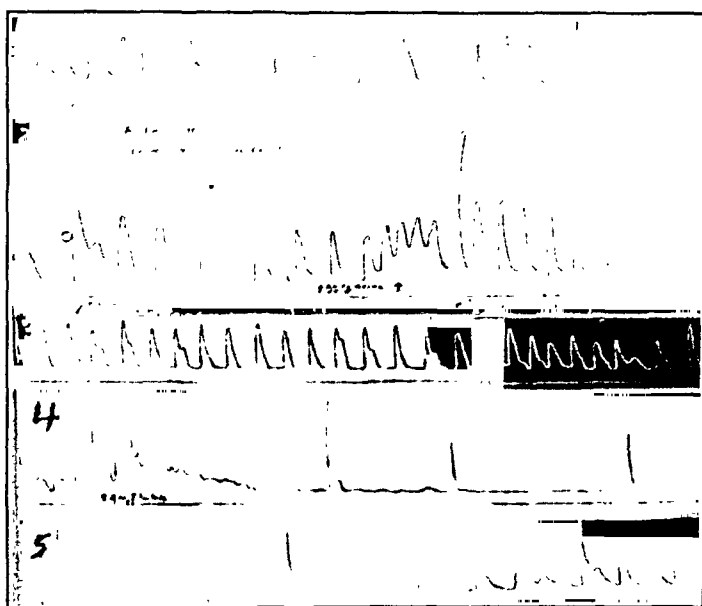


Fig. 6.—Response to urine in which the oxytocic phase (Tracing 2) was insignificant, the inhibitory phase positive, as indicated by slight gradual reduction in the amplitude of the rhythmical contractions and marked reduction in magnitude of response to pituitrin (Tracing 4) (compare with Fig. 4, Tracing 4).

Results obtained with urine from dysmenorrheic women were the exact reverse of those obtained with urine from women with no cramps with respect to: (1) the nature of effects characteristic of menstruation; and (2) the relation to menstruation and to the intermenstruum, respectively, of positive inhibitory effects and of responses in which *only* the inhibitory effect was positive.

The percentage of positive oxytocic effects was markedly greater, as compared with all other conditions, in association with dysmenorrhea (Chart I, complete graphs). Every specimen collected during the most severe phase of cramping, and 82.3 per cent of all specimens obtained during menstruation accompanied by dysmenorrhea, produced responses in which the oxytocic phase was positive. In the four groups of menstrual specimens, the percentages of positive oxytocic effects varied directly with the severity of the symptoms; in the intermenstrual groups, they were essentially equal.

Responses in which only the oxytocic phase was positive (Fig. 4) occurred with greatest frequency (Chart I, cross-hatched portions of graphs) after the injection of urine collected during the most severe phase of dysmenorrhea. Such responses were numerous throughout the cycle in dysmenorrheic women but were relatively infrequent in association with other conditions.

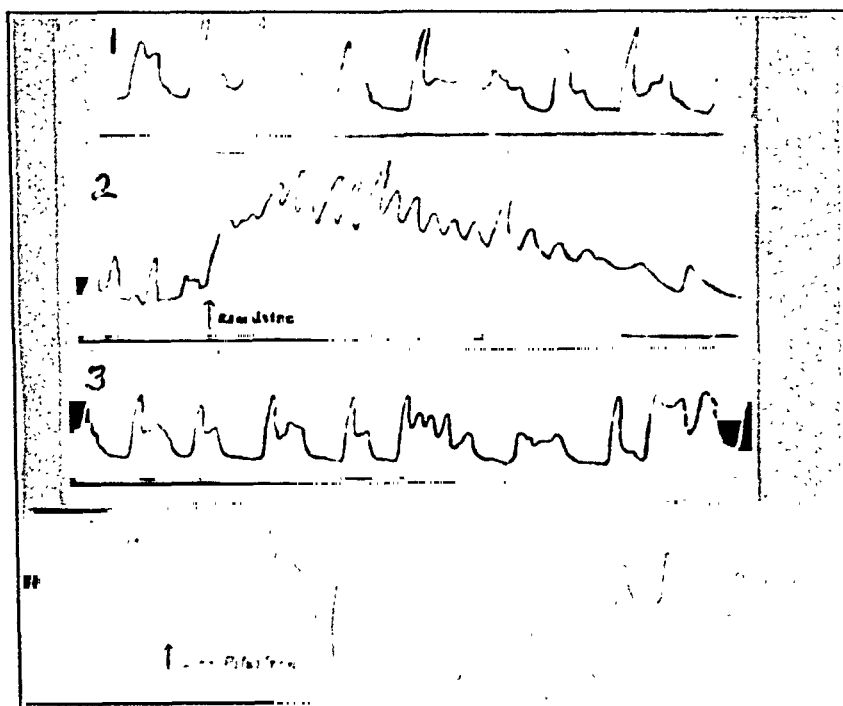


Fig. 4.—Response to urine (Tracing 2) in which the oxytocic phase was positive, the inhibitory phase negative (no reduction in subsequent motility or in response to pituitrin, Tracing 4).

The percentage of positive inhibitory effects was greatest in relation to menstruation accompanied by no cramps (Chart II, complete graphs). The percentages in the menstrual groups were inversely proportional to the severity of the symptoms; in the dysmenorrhea-menstrual groups they were significantly low as compared with all other groups.

Percentages of responses in which only the inhibitory phase was positive (Figs. 5 and 6) varied with the severity of symptoms as follows (Chart II, lined portions of graphs): inversely in the menstrual groups, and directly in the intermenstrual groups. No responses of this type were obtained with dysmenorrhea-menstrual specimens or with urine from men. As compared with all other conditions, the percentage was greatest in relation to menstruation accompanied by no cramps.

Responses in which both phases were positive (Fig. 3) occurred in all groups (Charts I and II, shaded portions of graphs); the percentage was highest in the case of specimens from men. The great majority of positive responses to urine

Pathologic or other special conditions were present in four of the individuals studied. The conditions present and the effects of the urine from these individuals are presented in Table II. It was of interest that after the relief of dysmenorrhea by presacral sympathectomy in one individual, cyclic variations were of the dysmenorrhea type.

DISCUSSION

It is apparent from the results obtained that human urine at times contains a substance or substances which affect uterine motility in the unanesthetized rabbit, producing a response in which an initial phase

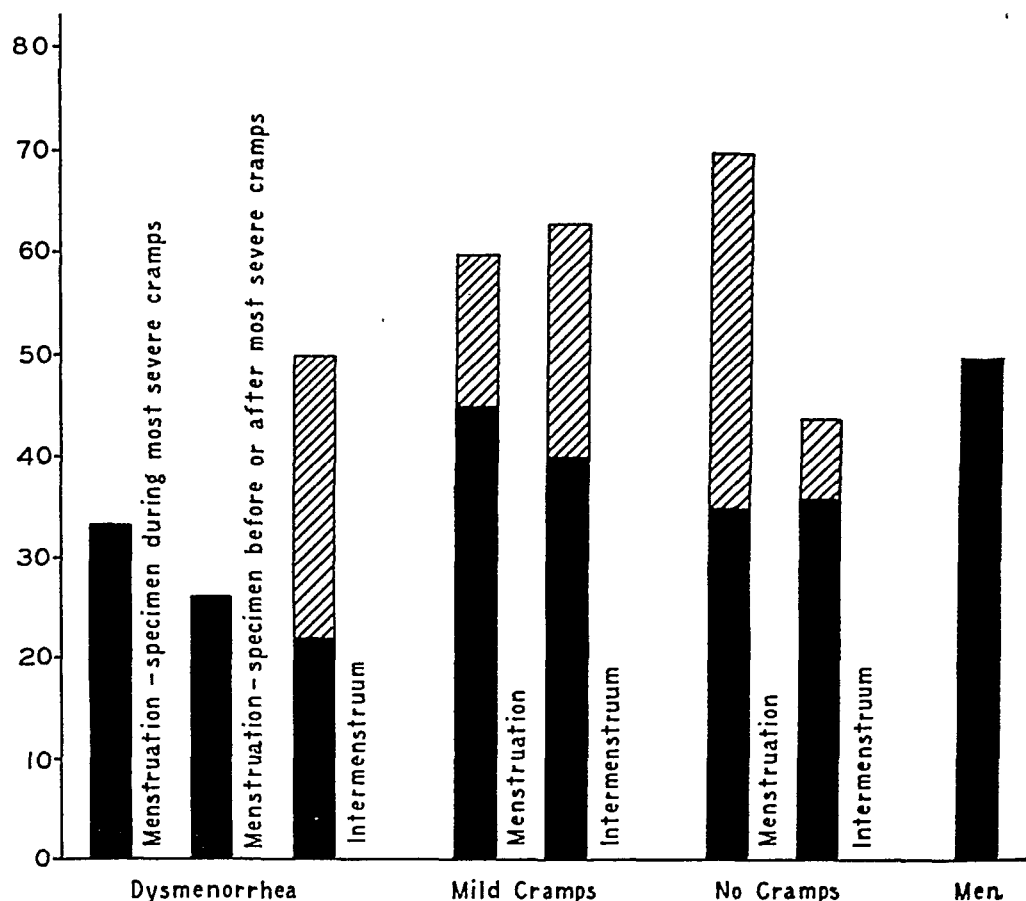


Chart II.—Distribution of positive inhibitory effects, considered separately, in relation to the conditions obtaining at time of collection of each specimen of urine. *Complete graphs:* Percentage of all specimens in each group producing positive inhibitory effects. *Lined portions of graphs:* Percentage of all specimens in each group producing responses in which the inhibitory phase was positive, the oxytocic phase absent or insignificant (Figs. 5 and 6). *Shaded portions of graphs:* Percentage of all specimens in each group producing responses in which both oxytocic and inhibitory phases were positive (Fig. 3).

of contraction is followed by evidence of an inhibitory effect. The responses produced by different specimens of urine from the same individual may vary widely in magnitude; further, the two phases of the response may vary in magnitude independently as well as simultaneously. Independent variations occur chiefly in women, and, with respect to nature and to occurrence in relation to the phases of the menstrual cycle, are definitely related to the degree of menstrual dis-

Menstrual and intermenstrual variations in the effects of urine from single individuals were of the nature indicated by the data as presented. There was some indication that effects could be further related to the phases of the intermenstruum; however, it was felt that the present material was insufficient for conclusions on this point. For these reasons, details of results in individual cases have not been presented. It should be noted that cyclic changes were as definite in the women with mild cramps as they were in the other women studied, but they varied in nature in different individuals. This explains the relatively insignificant variations in the percentages of positive oxytocic and inhibitory effects

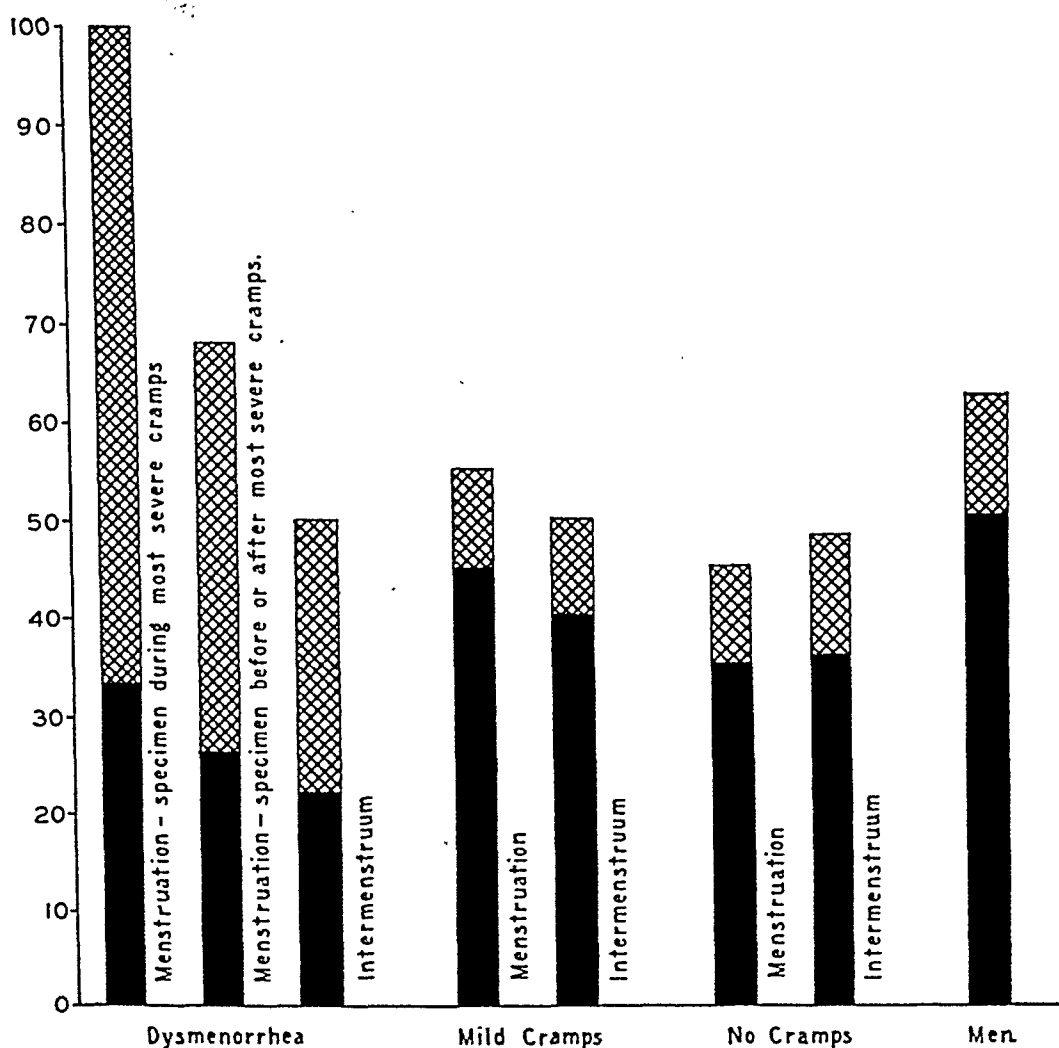


Chart 1.—Distribution of positive oxytocic effects, considered separately, in relation to the conditions obtaining at the time of collection of each specimen of urine. *Complete graphs:* Percentage of all specimens in each group producing positive oxytocic effects. *Cross-hatched portions of graphs:* Percentage of all specimens in each group producing responses in which the oxytocic phase was positive, the inhibitory phase absent or insignificant (Fig. 4). *Shaded portions of graphs:* Percentage of all specimens in each group producing responses in which both oxytocic and inhibitory phases were positive (Fig. 3).

in this group. In four of the cases studied, the discomfort experienced at different menstrual periods investigated varied in severity from dysmenorrhea to mild or no cramps. In every instance, the effects of the urine varied accordingly; they were predominantly oxytocic in association with dysmenorrhea, both oxytocic and inhibitory or predominantly inhibitory in association with mild or no cramps.

There may be a simultaneous increase in both effects at menstruation, or inhibitory effects may vary independently in relation to the cycle as in patients having no cramps or as in those with dysmenorrhea. In the latter case, corresponding variations in the oxytocic effect are lacking.

The nature of cyclic changes and the relative absence of predominantly oxytocic effects in individuals without dysmenorrhea indicate that dysmenorrhea is definitely associated with a marked oxytocic effect of the urine which is accompanied by relative absence of an inhibitory effect.

No attempt has been made to identify the active principle or principles present in the urine examined. However, the similarity of the effects of urine and of pituitrin is striking. It was shown by Reynolds^{17, 19} and by Weinstein and Friedman²⁰ that the initial contraction produced by pituitrin is due to the oxytocic factor, the subsequent inhibition, to the pressor factor. That the latter is able to reduce the sensitivity of the uterus without necessarily affecting the rhythmical motility was demonstrated by Weinstein and Friedman.²⁰

CONCLUSIONS

1. Human urine, when injected into rabbits, normally produces a response of the uterus in which an initial phase of contraction is followed by evidence of an inhibitory effect (reduction of spontaneous motility and decrease in the sensitivity of the uterus to pituitrin).

2. Urine excreted during normal menstruation shows an increase in the inhibitory activity, which is inversely proportional to the degree of discomfort present.

3. Urine excreted during dysmenorrheic cramping shows a marked increase in the oxytocic activity, together with a less marked, but significant, decrease in the inhibitory activity.

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comfort. Thus, in women without dysmenorrhea, such variations involve chiefly the inhibitory phase, whereas in women with dysmenorrhea, both phases are involved, the oxytocic to a greater degree. Further, independent variations occur throughout the cycle in dysmenorrheic women and, to a less extent, in women with mild cramps, but are largely confined to menstruation in women with no cramps.

Variations in the effects of urine from women, which are chiefly dependent upon independent variations in the two phases of the response, are definitely referable to menstrual and intermenstrual phases of the cycle. The nature of the cyclic changes is further referable to the degree of menstrual discomfort. Thus, in women with no cramps, there is at menstruation an increase in the degree of inhibition produced, with relatively little change throughout the cycle in the oxytocic effect. In women with dysmenorrhea, there is at menstruation an increase in the oxytocic effect, with a concurrent decrease in the degree of inhibition. The two effects tend to vary in inverse ratio throughout the cycle. In women with mild cramps, cyclic changes vary in different individuals.

TABLE II. EFFECTS OF URINE FROM INDIVIDUALS IN WHOM PATHOLOGIC OR OTHER SPECIAL CONDITIONS WERE PRESENT

CONDITION	NO. OF CASES	REMARKS	RESULTS
Essential hypertension	1	Dysmenorrhea of regular occurrence since onset of hypertension; no dysmenorrhea previously. Only one specimen of urine investigated.	The specimen, voided during the most severe phase of cramping, produced a response in which the oxytocic phase was positive, the inhibitory phase negative.
Postoperative (presacral sympathectomy for the relief of dysmenorrhea)	1	The menstrual period investigated began three days after operation, at the normally expected time. No cramps at this period. The specimen was obtained at the time when, previous to operation, cramps had been most severe. Three specimens investigated.	Menstrual specimen produced a response in which the oxytocic phase was positive, the inhibitory phase negative. Two intermenstrual specimens produced responses in which the oxytocic phase was negative or insignificant, the inhibitory phase positive.
Thyroid therapy for relief of dysmenorrhea	1	Urine collected during one complete cycle and parts of preceding and following cycles. Patient took 1 gr. of thyroid daily for 11 days before the onset of the second menstrual period. Dysmenorrhea was present at both periods.	Menstrual and intermenstrual variations in the effects of the urine were similar to those observed in other women with dysmenorrhea.
Spinal arthritis	1	The patient, a man, suffers pain frequently, but none was present at the time specimen was collected.	The specimen produced a response in which both oxytocic and inhibitory phases were positive.

toxemia. Ewing³ also noted that the location of the lesion did not disclose the severity of the symptoms. It would seem, therefore, that the underlying disturbance for the milder intoxication of pregnancy, namely vomiting, is probably a lesion in the liver similar to but of a milder degree than that seen in the more severe forms of toxemia of pregnancy.

ETIOLOGY

Numerous theories have been advanced regarding the etiology of this vomiting, varying to include maternal, fetal, placental, endocrine, chemical, and dietary disturbances. We feel that it is beyond the scope of this paper to discuss the all too many conflicting points of view regarding the etiology of this condition, but shall confine ourselves to those having a direct bearing on the problem at hand. Whether disturbances in the carbohydrate metabolism exist or are of primary etiologic significance is not clear. The opinions regarding this are conflicting. That treatment with glucose, however, is beneficial in many cases of vomiting can be undisputed. It is possible that an altered carbohydrate metabolism may be dependent on a primary liver damage similar to the carbohydrate disturbance found by Minot and Cutler⁵ in their dogs where liver damage was produced by carbon-tetrachloride poisoning. In this latter situation the liver lesion is similar to that occurring in the toxemias of pregnancy. It has also been demonstrated in phosphorous poisoning that there is a disappearance of glycogen from the liver which can be replenished by sugar feeding. And furthermore, the toxic manifestations of carbontetrachloride poisoning can likewise be relieved by sugar therapy. It would seem, therefore, by analogy that high carbohydrate feeding would be indicated in the toxemias of pregnancy where liver damage is also present.

Much has been written regarding the alterations of calcium metabolism both in the normal and in the toxemic states of pregnancy. From the large mass of conflicting data, Stander¹ states that one cannot conclude that a decrease in the total blood calcium or in the dialyzable blood calcium is associated with eclampsia. These blood findings, however, do not necessarily reveal the complete story regarding the calcium metabolism. It has been frequently demonstrated that the level of calcium in the blood does not parallel the degree of calcium retention in the tissues. Calcium has been advocated in the treatment of the toxemias of pregnancy. The rationale for the use of this salt is dependent upon the finding by many observers of a lowered blood calcium in eclampsia and upon the analogy that convulsions occur both in eclampsia and in the hypocalcemia of tetany. But, as mentioned above by Stander, lowering of the blood calcium is not a consistent finding in eclampsia or in the other toxemias and, therefore, any bene-

THE USE OF PARATHYROID EXTRACT IN THE CONTROL OF EARLY NAUSEA AND VOMITING OF PREGNANCY*

A PRELIMINARY REPORT

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NAUSEA and vomiting are generally considered necessary accompaniments of early pregnancy and must be tolerated in varying severity until life is felt. According to Stander¹ this vomiting occurs in 50 per cent of all pregnancies. Our records indicate that vomiting might begin as early as the first week of gestation; however, it usually commences during the second week. This syndrome is characterized by slight or moderate nausea and is most often associated with the vomiting of a bile-stained foamy fluid, following which the patient immediately feels a sense of relief. The nausea and vomiting usually last for three and a half to four and a half months but occasionally persist throughout gestation. In cases where this mild type of toxemia does not abate the condition may gradually progress to the more severe types of toxemia.† Strauss² aptly emphasized that the vomiting of early pregnancy is never a physiologic process, but is the expression of some pathologic state whether neurotic or toxic, always dangerous and threatening.

PATHOLOGY

The similarity of the pathologic lesions in hyperemesis to those of eclamptic toxemia have been pointed out by Ewing³ who demonstrated that in both situations the fundamental lesion is necrosis of the liver cells. Some observers have contrasted the central lobule necrosis seen in cases of vomiting in pregnancy with the peripheral zone necrosis of eclampsia, and have considered this pathologic difference to be indicative of an etiological difference. Davidson,⁴ however, discussing the pathology of eclampsia and puerperal toxemia, states that in some instances of severe toxemia there is involvement of the peripheral zones, in others widespread central and midzone necrosis, and in still others no gross hepatic lesions but only small areas of focal necrosis. This demonstrates, we believe, that the location of the lesion in the liver is of no diagnostic significance in differentiating the types of

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†The following classification of toxemias is given by Stander:¹ (1) vomiting of pregnancy, (2) low reserve kidney, (3) nephritis complicating pregnancy, (4) pre-eclampsia, (5) eclampsia, and (6) acute yellow atrophy of the liver.

EXPERIMENTAL DATA

The patients in this study were divided into two groups. All patients in both groups were placed on a diet high in carbohydrates, low in fat, and with restricted condiments. The patients in Group I were given orally about 40 gr. of calcium daily, usually in the form of phosphate, 10 c.c. of a 10 per cent solution of calcium gluconate intravenously at varying intervals. The patients in Group II were given the calcium orally and 100 units of parathyroid extract in some cases intramuscularly and in others intravenously every two or three days. A few of the patients in the second group were also given calcium gluconate parenterally.

Since these patients were from private practice, it was difficult in many of them to get full cooperation. In the first place, many of them reported after vomiting had been established for many days and often were unable to recall accurately how long nausea and vomiting had existed. Second, it was difficult to get them to come in for injections at frequent intervals. Third, it was not possible to determine

TABLE I

CASE	GRAVIDA	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF CALCIUM GLUCONATE INJECTIONS
JL-1	ii	47 days	61st day	14 days	4 each 10 c.c.
SM-2	ii	78 days	94th day	16 days	7 each 10 c.c.
SS-3	i	67 days	110th day	43 days	6 each 10 c.c.
LS-4	i	71 days	78th day	7 days	4 each 10 c.c.
EB-6	i	110 days	200th day	90 days	9 each 10 c.c.
MK-7	i	104 days	124th day	20 days	2 each 10 c.c.
RK-8	i	74 days	83rd day	9 days	3 each 10 c.c.
CK-9	ii	66 days	76th day	10 days	2 each 10 c.c.
RS-10	i	72 days	95th day	23 days	5 each 10 c.c.
DG-11	i	56 days	114 days	58 days	11 each 10 c.c.
BC-12	i	47 days	89th day	42 days	4 each 10 c.c.
EI-13	i	56 days	90th day	34 days	11 each 10 c.c.

First and Second Months

JL-1	ii	47 days	61st day	14 days	4 each 10 c.c.
DG-11	i	56 days	114 days	58 days	11 each 10 c.c.
BC-12	i	47 days	89th day	42 days	4 each 10 c.c.
EI-13	i	56 days	90th day	34 days	11 each 10 c.c.

Third and Fourth Months

SM-2	ii	78 days	94th day	16 days	7 each 10 c.c.
SS-3	i	67 days	110th day	43 days	6 each 10 c.c.
LS-4	i	71 days	78th day	7 days	4 each 10 c.c.
RK-8	i	74 days	83rd day	9 days	3 each 10 c.c.
CK-9	ii	66 days	76th day	10 days	2 each 10 c.c.
RS-10	i	72 days	95th day	23 days	5 each 10 c.c.
EB-6	i	110 days	200th day	90 days	9 each 10 c.c.
MK-7	i	104 days	124th day	20 days	2 each 10 c.c.

ficial effect of calcium therapy in the intoxications of pregnancy might have an influence aside from restoring the blood calcium to a normal level. A relationship between the disturbances in calcium metabolism and carbohydrate metabolism has been demonstrated in many ways. Minot and Cutler⁵ found that the hypoglycemia associated with the liver damage produced by carbontetrachloride poisoning was relieved when calcium was administered. These authors quote Underhill and Blatherwick⁶ as having demonstrated a hypoglycemia following parathyroidectomy where the blood sugar was raised by calcium therapy. The relief of the hypoglycemia and other symptoms of intoxication from carbontetrachloride poisoning by calcium therapy observed by the above-mentioned authors occurred even though there was no evidence of a reduced blood calcium during the toxic state. Since the liver pathology in the vomiting of pregnancy, where central necrosis is found, is similar to that described for carbontetrachloride poisoning, it would seem that a beneficial action of calcium therapy in the former situation would be similar to its effect in carbontetrachloride poisoning, that is, an influence on the carbohydrate metabolism.

It is understandable, in the light of recent work, why calcium therapy has been of so little value in the convulsions of eclampsia. It is known that the normal response of an animal to parathyroid administration is a rise in the blood calcium. This rise, as Nitzescu⁷ has shown, is greatly diminished in the presence of liver damage produced by phosphorous poisoning. Greenberg⁸ found a similar but less striking failure of the blood calcium to rise after parathormone administration when liver damage was produced with hydrazine. It would therefore appear that the liver damage as seen in the toxemias of pregnancy might interfere not only with the carbohydrate but also with the calcium metabolism of the body. The normal influence of the parathyroid gland in maintaining a proper balance of calcium in the body may not be operative in these circumstances of liver damage.

Calcium therapy alone, and this has likewise been Nixon's⁹ experience, was not greatly beneficial in the treatment of the vomiting in pregnancy. *Since calcium therapy alone was ineffectual in relieving the symptoms of this intoxication, and since, as Nitzescu⁷ observed, the normal action of the parathyroid gland is disturbed during liver damage, it occurred to us that a combination of calcium and parathyroid extract, where these two substances could be supplied in amounts larger than usual to the tissues, might be of value in the treatment of this mild intoxication.* Further study confirmed this supposition. Lopez,¹⁰ using parathyroid hormone in the treatment of eclampsia, noted the disappearance of the toxic symptoms as well as the convulsions following its use. As far as we can determine, this therapy has not been heretofore applied to the mild toxemias.

TABLE II—CONT'D

CASE	GRAVIDA	AGE OF PREG- NANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOM- ATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF PARATHYROID EXTRACT INJECTIONS GIVEN
<i>First and Second Months—Cont'd</i>					
SG-43	i	15 days	18 days	3 days	3 each 1 c.c. 3 cal. gluc.
RS-44	i	42 days	44 days	2 days	2 each 1 c.c. 2 cal. gluc.
JS-45	ii	42 days	44 days	2 days	1 each 1 c.c. 1 cal. gluc.
RH-46	i	63 days	67 days	4 days	4 each 1 c.c. 4 cal. gluc.
SL-47	i	61 days	66 days	5 days	5 each 1 c.c. 5 cal. gluc.
SL-48	i	55 days	57 days	2 days	2 each 1 c.c. 2 cal. gluc.
RF-49	ii	56 days	61 days	5 days	4 each 1 c.c. 4 cal. gluc.
RL-50	i	61 days	64 days	3 days	3 each 1 c.c. 3 cal. gluc.
PM-51	i	58 days	60 days	2 days	2 each 1 c.c. 2 cal. gluc.
<i>Third and Fourth Months</i>					
FG-52	i	65 days	88 days	23 days	9 each 1 c.c.
SL-53	i	81 days	90th day	9 days	5 each 1 c.c.
RA-54	i	61 days	75th day	14 days	4 each 1 c.c.
EL-55	i	125 days	157th day	32 days	9 each 1 c.c.
FF-56	ii	127 days	129 days	2 days	1 each 1 c.c.
EN-57	ii	77 days	86 days	9 days	5 each 1 c.c.
VK-58	i	92 days	94th day	2 days	1 each 1 c.c. 1 cal. gluc.
SC-59	i	109 days	118 days	9 days	4 each 1 c.c.
CR-60	i	105 days	113 days	8 days	4 each 1 c.c.
MP-61	i	78 days	92 days	14 days	5 each 1 c.c.
RL-62	i	69 days	116th day	47 days	13 each 1 c.c.
HC-63	i	65 days	71st day	6 days	4 each 1 c.c.
RZ-64	i	48 days	70 days	22 days	11 each 1 c.c.
RO-65	i	73 days	95th day	22 days	16 each 1 c.c.
RR-66	i	91 days	111th day	20 days	6 each 1 c.c.
IB-67	i	110 days	113 days	3 days	3 each 1 c.c.
AL-68	i	74 days	81 days	7 days	3 each 1 c.c.
SP-69	ii	67 days	70th day	3 days	2 each 1 c.c.
MM-70	i	110 days	128th day	18 days	4 each 1 c.c.
MR-71	ii	89 days	94th day	5 days	3 each 1 c.c.
RB-72	ii	81 days	92 days	11 days	3 each 1 c.c. 4 cal. gluc.
VB-73	ii	94 days	96 days	2 days	2 each 1 c.c.
FE-74	i	75 days	79 days	4 days	2 each 1 c.c. 2 cal. gluc.
ET-75	i	86 days	95th day	9 days	7 each 1 c.c. 5 cal. gluc.
ES-76	i	73 days	75 days	2 days	2 each 1 c.c. 2 cal. gluc.
AB-77	ii	72 days	77th day	5 days	2 each 1 c.c. 2 cal. gluc.
EH-78	v	72 days	76th day	4 days	2 each 1 c.c.
DW-79	i	118 days	121 days	3 days	4 each 1 c.c. 4 cal. gluc.

TABLE II

CASE	GRAVIDA	AGE OF PREG- NANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOM- ATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF PARATHYROID EXTRACT INJECTIONS GIVEN
<i>First and Second Months</i>					
BJ-1	i	51 days	61st day	10 days	5 each 1 c.c.
LS-2	i	61 days	78th day	17 days	4 each 1 c.c.
JF-3	i	52 days	60th day	8 days	1 each 1 c.c.
MK-4	ii	56 days	67th day	11 days	3 each 1 c.c.
RG-5	i	55 days	78th day	23 days	10 each 1 c.c.
RG-6	ii	52 days	58 days	6 days	3 each 1 c.c.
JF-7	i	60 days	70 days	10 days	4 each 1 c.c.
SL-8	i	55 days	77 days	22 days	6 each 1 c.c.
ES-9	i	49 days	52nd day	3 days	3 each 1 c.c.
CL-10	i	50 days	78th day	28 days	12 each 1 c.c.
OL-11	ii	36 days	71st day	35 days	7 each 1 c.c.
ES-12	i	51 days	67th day	16 days	2 each 1 c.c. 2 cal. gluc.
EN-13	i	53 days	55 days	2 days	2 each 1 c.c.
MT-14	i	42 days	57 days	15 days	2 each 1 c.c. 2 cal. gluc.
TM-15	i	34 days	38 days	4 days	3 each 1 c.c.
HD-16	i	59 days	67th day	8 days	2 each 1 c.c.
RC-17	i	64 days	87th day	23 days	6 each 1 c.c.
EC-18	i	36 days	38th day	2 days	1 each 1 c.c. 1 cal. gluc.
BS-19	i	40 days	46th day	6 days	4 each 1 c.c.
MP-20	i	44 days	68 days	24 days	5 each 1 c.c.
GG-21	i	54 days	92 days	38 days	7 each 1 c.c. 7 cal. gluc.
SM-22	i	40 days	56th day	16 days	4 each 1 c.c.
SS-23	i	62 days	79th day	17 days	7 each 1 c.c.
EG-24	iii	41 days	64th day	23 days	8 each 1 c.c.
SF-25	i	54 days	84th day	30 days	6 each 1 c.c.
ET-26	i	54 days	68th day	14 days	8 each 1 c.c.
AC-27	ii	55 days	57 days	2 days	2 each 1 c.c.
SC-28	ii	50 days	57 days	7 days	7 each 1 c.c.
LV-29	i	51 days	72nd day	21 days	6 each 1 c.c.
AC-30	i	54 days	60th day	6 days	3 each 1 c.c.
NF-31	i	66 days	70th day	4 days	3 each 1 c.c.
MA-32	ii	44 days	85th day	41 days	14 each 1 c.c.
EY-33	i	41 days	61st day	20 days	3 each 1 c.c.
PB-34	i	62 days	96 days	34 days	9 each 1 c.c. 9 cal. gluc.
CG-35	ii	45 days	58 days	13 days	3 each 1 c.c. 3 cal. gluc.
CP-36	ii	43 days	57 days	14 days	2 each 1 c.c. 4 cal. gluc.
HG-37	i	49 days	53 days	4 days	3 each 1 c.c. 3 cal. gluc.
RB-38	i	51 days	59 days	8 days	3 each 1 c.c. 3 cal. gluc.
LR-39	ii	52 days	59 days	7 days	2 each 1 c.c. 3 cal. gluc.
HO-40	i	63 days	80 days	17 days	6 each 1 c.c. 4 cal. gluc.
JF-41	i	41 days	43 days	2 days	2 each 1 c.c. 2 cal. gluc.
GK-42	i	53 days	59 days	6 days	2 each 1 c.c. 2 cal. gluc.

TABLE III B. COMPARATIVE FIGURES OF TABLES I AND II (THIRD AND FOURTH MONTHS OF PREGNANCY)

	NUMBER OF CASES	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NUMBER OF INJECTIONS
Calcium gluconate	8	80.3	107.5	27.2	4.5
Parathyroid extract	37	84.3	93.7	9.4	4.4

TABLE III C. COMPARISON OF ENTIRE TABLE I AND ENTIRE TABLE II

	NUMBER OF CASES	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NUMBER OF INJECTIONS
Calcium gluconate	12	70.6	101	30.5	5.7
Parathyroid extract	88	64.8	76	11.2	4.5

nancy. In Group II there were three patients who were not included in the latter tables; in these the parathyroid extract and calcium failed to control the vomiting.

THREE CASES NOT RESPONDING TO ANY TYPE OF TREATMENT

KY-SPECIAL I.—

Physical Examination: Primigravida, aged twenty-six years, married four years, weight 114 pounds, height 5 feet 4 inches, heart and lungs negative, pelvic measurements normal. Wassermann negative.

Menstrual History: Thirteen $\frac{35 \text{ day}}{6-7 \text{ day}}$ slight pain lower abdomen few days before and stops with onset; moderate flow, mostly second day, no clots. Last menstrual period October 16. Due: July 23.

Personal History: No miscarriages, tonsils and adenoids removed in childhood, pelvic abscess operation.

Present Complaints: (1) Nausea and vomiting (three times a day), (2) burning feeling and bitter taste in mouth, (3) frequent urination, and (4) best weight 113 pounds.

Vaginal Examination: Primiparous vagina, uterus enlarged commensurate with period of amenorrhea.

Summary of Prenatal Care.—(1) Urine for last five months of pregnancy at times showed a trace of albumin and occasional hyaline cast. (2) Blood pressure varied from $\frac{120 \text{ to } 128 \text{ systolic}}{80 \text{ to } 90 \text{ diastolic}}$. (3) Increase in weight 18 pounds, gain regular without losses. (4) Fifteen injections (1 c.c. each) of parathyroid extract given. (5) All types of treatment given. (6) Calcium taken irregularly. Patient felt no medicine or food agreed with her. (7) Delivered of a male child.

TABLE II—CONT'D

CASE	GRAVIDA	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF PARATHYROID EXTRACT INJECTIONS GIVEN
<i>Third and Fourth Months—Cont'd</i>					
FZ-80	i	71 days	74th day	3 days	2 each 1 c.c.
EG-81	i	67 days	74 days	7 days	3 each 1 c.c.
PB-82	i	89 days	92 days	3 days	3 cal. gluc.
RS-83	i	88 days	90 days	2 days	3 each 1 c.c.
FM-84	i	70 days	72 days	2 days	3 cal. gluc.
PS-85	ii	103 days	107 days	4 days	2 each 1 c.c.
PL-86	i	77 days	81 days	4 days	2 cal. gluc.
BF-87	i	89 days	91 days	2 days	3 each 1 c.c.
DR-88	i	78 days	84 days	6 days	3 cal. gluc.
					2 each 1 c.c.
					6 cal. gluc.
					6 each 1 c.c.

accurately how much calcium they actually took by mouth. In general, however, the patients cooperated very well in this study.

A summary of the results of the twelve patients in the first group is given in Table I. Table II is a summary of the 88 patients in Group II. The data presented in Tables I and II demonstrated the superiority of parathyroid extract plus calcium over calcium alone and over the usual accepted therapy. The tables clearly indicate a definite shortening of the duration of the early vomiting of pregnancy by this treatment. Whereas in Group I (Table I), the nausea and vomiting persisted on an average of 30.5 days after treatment was instituted with an average of 101 days in pregnancy, Group II, Table II, where parathyroid extract was used along with calcium the symptoms persisted on an average of only 11.2 days with an average of 76 days in preg-

TABLE III A. COMPARATIVE FIGURES OF TABLES I AND II (FIRST AND SECOND MONTHS OF PREGNANCY)

	NUMBER OF CASES	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NUMBER OF INJECTIONS
Calcium gluconate	4	51.5	88.5	37.0	7.5
Parathyroid extract	51	50.5	63.2	12.7	4.3

tract, we do not wish to create the impression that we feel that other sound therapeutic measures should be neglected in the handling of such patients but we offer this as an additional therapeutic procedure.

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1900 RITTENHOUSE SQUARE

DISCUSSION

DR. JOHN McGLINN.—Many of the cases which show not the ordinary nausea of pregnancy but the true hyperemesis of the early months of pregnancy, do develop the toxemia of the later months. Dr. Missett presented a series of cases several years ago, showing a greater than average incidence of toxemia among the cases which had had marked hyperemesis in the early stages of pregnancy.

We have all tried the various forms of treatment for nausea and vomiting of the early months of pregnancy. We were enthralled, for example, at one time with the use of corpus luteum, a most irrational treatment. Yet I know from the full series of cases which Sussman has studied that he has undoubtedly added something in the combination of calcium and parathyroid in the treatment of this condition which is of distinct value. The treatment he has presented deserves a trial by the members of this Society.

DR. COLLIN FOULKROD.—Are we to gather from this paper that the lowering of the calcium of the blood will lead to eclampsia if allowed to go untreated? The lowered calcium in the blood is replenished, as I understand it, by the action of parathyroid hormone drawing the calcium from the body stores. This hormone does not absorb or help introduce new calcium into the tissues. Calcium is absorbed by the action of vitamin D and a normal balance is maintained by carrying off the excess in urine and feces.

From some writings I am led to believe that the use of parathyroid hormone in too large quantities might lead to a *drawing-off* of the calcium from the bones in too great quantity. Yet if you can give an active supply in the food while giving parathyroid hormone, it is quite likely there will be no over-reduction in the bones and other parts of the body of the woman.

I do not believe corpus luteum was a failure in the treatment of nausea of pregnancy. Certain patients need thyroid extract, or extract of corpus luteum to become pregnant, and some also need these glandular extracts throughout pregnancy so that they may continue to full term. Individuals vary in their requirements, and there are a number who are promptly relieved by the use of corpus luteum in the toxemia of pregnancy.

A better form of control would compare the bed day results of the glucose injection method or a modified Titus treatment, and the parathyroid method, to see if the days in bed could be lessened by this proposed new method. We all know that those patients who go to a hospital and accept a modified form of sedative and glucose therapy can be relieved in a few days.

NR-SPECIAL II.—

Physical Examination: Multipara ii, aged thirty years, married seven years, two pregnancies; instrumental; weight $122\frac{1}{2}$ pounds, height 5 feet $5\frac{1}{4}$ inches, blood pressure 110/80, pelvic measurements normal, Wassermann, chemistry and blood count normal.

Menstrual History: Twelve $\frac{28 \text{ days}}{3 \text{ days}}$ no pain, scant flow, mostly second day, small clots occasionally, last menstrual period April 4. Due: January 9.

Personal History: Diphtheria early childhood, scarlet fever at nineteen years of age, appendix out 1924, second child died at nine months of age (pneumonia?).

Present Complaints: (1) Nausea and vomiting, (2) moderately constipated, (3) restless, (4) headaches off and on, and (5) best weight 125 to 128 pounds.

Vaginal Examination: Rectocele, cystocele, lacerated cervix, uterus enlarged commensurate with period of amenorrhea.

Summary of Prenatal Care: (1) Urine negative throughout pregnancy. (2) Blood pressure varied from $\frac{100 \text{ to } 120 \text{ systolic}}{70 \text{ to } 80 \text{ diastolic}}$. (3) Increase in weight $14\frac{3}{4}$ pounds, gain was regular without any losses. (4) Nine injections parathyroid extract given. (5) All known effective home treatment given. (6) Vomiting aggravated at approximately time of month that period would have been due. (7) Delivered of male child.

RR-SPECIAL III.—

Physical Examination: Primigravida, aged twenty-two years, married one and one-half years, height 5 feet $4\frac{1}{2}$ inches, weight 116 pounds, blood pressure 110/70, acne vulgaris of face, eyes refracted, lungs negative, heart—aortic systolic murmur referred to vessels right side of neck, pelvic measurements normal. Wassermann negative.

Menstrual History: Thirteen $\frac{7 \text{ to } 8 \text{ weeks}}{8 \text{ days}}$ until marriage $\frac{28 \text{ days}}{6 \text{ days}}$. Occasional cramps in lower abdomen, moderate to profuse flow mostly second and fourth days, small clots. Last menstrual period June 26. Due: April 2.

Personal Examination: No miscarriages, tonsils out age nine years, cystic ovary (according to previous examination by physician).

Present Complaints: (1) Nausea and vomiting, (2) frequent urination, and (3) cramps July 1, no bleeding.

Vaginal Examination: Primiparous vagina, uterus enlarged commensurate with period amenorrhea.

Summary of Prenatal Care: (1) Urine normal throughout. (2) Blood pressure varied from $\frac{100 \text{ to } 122 \text{ systolic}}{60 \text{ to } 80 \text{ diastolic}}$. (3) Increased weight $23\frac{1}{2}$ pounds, gained regularly up to fourth month, then lost three pounds, thereafter gained regularly until delivery. (4) Twenty injections parathyroid extract. (5) Nauseated for two weeks after life was felt, morning nausea until term. (6) Calcium taken irregularly, nausea less when injection parathyroid extract was taken. (7) Delivered of female child.

CONCLUSIONS AND SUMMARY

From the data presented it seems fair to conclude that parathyroid extract along with calcium therapy is of distinct value in controlling the early nausea and vomiting of pregnancy. From experimental data there is a rationale for the use of this extract. Whether, as suggested by Lopez,¹⁰ parathyroid extract will be of value in the late toxemias of pregnancy can be demonstrated only by future investigation. In presenting this treatment of the early toxemias with parathyroid ex-

METHODS

On all patients frequent examinations were made of blood pressure, eyegrounds, blood chemistry, urine, and kidney function.

Complete mixed twenty-four-hour urine specimens were collected and refrigerated until extracted.

There was no attempt to select the cases for study. Urine specimens were obtained as the patients, not in labor, but in the last trimester of pregnancy, were admitted to the University Hospital. Therefore, the normal controls were scattered among the toxemic cases.

Most patients were service cases; few private cases were included. Nearly all patients reported to our prenatal clinic for from one to six months previous to admission to the hospital.

No cases of true eclampsia appear in this series because of their incontinence which rendered impossible the collection of complete twenty-four-hour urine specimens.

PROCEDURE

The test devised by Schmulovitz and Wylie⁶ for the chemical diagnosis of pregnancy by the detection of estrin in the urine was used in all the cases in this series. The reader is referred to their original paper for full details. Briefly their method "... consists in the extraction of estrin from the urine with ether and its detection by coupling with diazotized para-nitroaniline to form a deep-colored azo dye. . . ."⁶ In our procedure certain modifications were made in the original technic, as follows:

1. The urine specimens were hydrolyzed at pH 2 instead of pH 4. This was done because it was felt that there was more complete hydrolysis at pH 2.

2. The specimens were evaporated to 400 c.c. rather than to 200 c.c. This was made possible by using a new type, and larger, extraction flask, resulting in a saving of time.

3. The urines were ether-extracted at pH 2 rather than at pH 1 because it was found by Schmulovitz⁵ that further acidification beyond that of hydrolysis gave no increased yields of hormone.

4. After completion of the steam distillation to remove the volatile phenols, the hormone residue was obtained by partial vacuum distillation, instead of removing the water by heating in a glycerin bath at 160° C., because of the time thus saved.

The procedure otherwise was as outlined in the original paper.⁶ An improved combined extractor and extract-washer, as described in a later publication by Wylie and Schmulovitz,¹⁴ was used in all our experiments. Each specimen in this entire series was subjected to exactly the same procedure.

The "ferrie chloride number" (F.N. as shown in Tables I to V) is obtained as follows: the final colored alcoholic layer containing the estrin extracted from the specimen is filtered into a colorimeter cup and set at 10 mm., and is compared with a standard 33 per cent ferrie chloride solution, the reading of which is the "ferrie chloride number." A F.N. of 25 or more is considered by Schmulovitz and Wylie⁶ as posi-

DR. LEON ISRAEL.—I would like to ask Dr. Sussman if he knows if any abnormal reaction from the use of parathyroid and calcium has been reported, and whether, after withdrawal of the treatment, there was any recurrence of nausea and vomiting?

DR. SUSSMAN (closing).—No abnormal reaction has been noted in my cases. A standardized parathyroid extract has been used throughout. In the cases of calcium gluconate the injected material was produced by a fermentative instead of the chemical method. Except in the intractable cases mentioned there was no recurrence of nausea and vomiting.

The hormonal effect of parathyroid extract is stressed in this thesis, which is of a different nature from that usually attributed to calcium and vitamin "D" relationship. There were no bed cases included in this report.

A CHEMICAL TEST FOR PREGNANCY APPLIED TO THE DETERMINATION OF ESTRIN IN THE URINE OF NORMAL AND TOXEMIC PATIENTS IN THE LAST TRIMESTER OF PREGNANCY

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University of Maryland)

THERE are widely divergent opinions concerning the levels of estrin in blood and urine in the late toxemias of pregnancy. Smith and Smith⁸⁻¹¹ found a tendency toward low estrin levels in the blood and urine. Heim² obtained values much greater than normal for estrin excretion in the urine in a small series of cases. Bickenbach and Fromme¹ found normal estrin values in the blood, while Runge and Diethelm⁴ showed a lowered estrin excretion in the urine in their small series of cases of the late toxemias. All of these estimations were based on bio-assay methods.

Since it was desired to eliminate as many as possible of the variable biologic factors, a chemical test for pregnancy, described by Schmulovitz and Wylie,⁶ was used in this investigation of estrin excretion in the urine of patients suffering from the late toxemias of pregnancy. By means of this test we have been able to establish levels of estrin excretion in normal late pregnancy, and also to show a definite lowering of these levels in chronic nephritis complicating pregnancy, and in preeclampsia.†

*Charles M. Hitchcock Fellow in Obstetrics.

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†The absence of a universally accepted classification of the toxemias of pregnancy is a hindrance to proper correlation of the observations of various workers in this field. It is for this reason that we must give the classification of the late toxemias of pregnancy as accepted in our clinic. By the term late toxemias of pregnancy we refer to: preeclampsia, eclampsia, and chronic nephritis complicating pregnancy. With Irving⁷ we agree that preeclampsia should not be subdivided into a mild and severe group. This is at variance with Stander^{12,13} who divides the so-called preeclamptic toxemia into "low reserve kidney" and preeclampsia. Thus we have included under the heading of preeclampsia all cases which, in Stander's classification would be subdivided into "low reserve kidney" and preeclampsia.

was obtained for analysis, "ferrie chloride number" (F.N.), and the outcome of the pregnancy (F.T.L., full-term living baby; L, premature baby who survived the neonatal period; and D, premature baby who was stillborn, or born alive but did not survive the neonatal period). Tables IV and V are summaries of the data shown in Tables I to III.

TABLE III. TWENTY CASES OF PREECLAMPSIA

CASE NO.	AGE	COLOR	PARITY	DURATION OF PREG. WHEN URINE OBT.	F.N.	BABY
5	27	W	0-0-0-0	38	45.5	F.T.L.
36	18	B	0-0-0-0	40	44.5	F.T.L.
40	16	B	0-0-0-0	39	42.0	F.T.L.
35	29	W	0-0-0-0	37	40.5	37D
60	14	B	0-0-0-0	34	40.0	F.T.L.
23	23	W	0-0-0-0	38	39.0	F.T.L.
63	21	W	0-0-0-0	40	38.5	F.T.L.
45	60	B	0-0-0-0	40	38.5	F.T.L.
37	28	B	0-0-0-0	40	38.0	F.T.L.
49	21	B	0-0-0-0	39	37.5	F.T.L.
66	19	W	0-0-0-0	40	37.2	F.T.L.
61	16	W	0-0-0-0	36	36.5	F.T.L.
10	19	W	0-0-0-0	40	35.5	F.T.L.
9	21	B	1-0-0-0	40	35.0	F.T.L.
64	24	W	0-0-0-0	40	34.5	F.T.L.
57	14	W	0-0-0-0	40	33.4	F.T.L.
48	21	B	0-0-0-0	32	32.0	F.T.L.
65	18	B	0-0-0-0	38	31.0	F.T.L.
22	17	B	0-0-0-0	34	30.0	34D
24	16	B	0-0-0-0	38	28.5	F.T.L.

TABLE IV. SUMMARY—TABLES I, II, III

	AVERAGE F.N.	F.N. RANGE	TOTAL NO. OF CASES	AVERAGE DURA- TION OF PREGNANCY, WEEKS
Normal	83.30	152.00-56.60	21	36.0
Chronic nephritis compli- cating pregnancy	51.67	64.00-40.00	19	37.1
Preeclampsia	36.87	45.00-28.50	20	38.1

In Tables I to III the parity of the patient is expressed in 4 figures according to a compact scheme, the origin of which is not known. The first figure represents the number of full-term children the patient has borne whether born alive or stillborn; the second figure gives the number of premature babies the patient has borne whether born alive or stillborn; the third figure indicates the number of abortions (termination of pregnancy on or before the twenty-eighth week); while the fourth figure shows the number of living children the patient has. In designating the parity of these patients by this method, the present pregnancy which has been studied has not been included, thus a primigravida is shown as a para 0-0-0-0.

tive for pregnancy. These investigators' ultimately hope to correlate their chemical test and the biologic assays by converting "ferrie chloride numbers" into milligrams of estrin and rat units. This work is in progress.

DISCUSSION

In Tables I to III the data are arranged under the following headings: case number, age, color, parity of the patient, duration of pregnancy in weeks at the time when the twenty-four-hour specimen of urine

TABLE I. TWENTY-ONE NORMAL CASES

CASE NO.	AGE	COLOR	PARITY	DURATION OF PREG. WHEN URINE OBT.	F.N.	BABY
29	21	W	0-0-0-0	36	152.0	F.T.L.
25	21	W	0-0-0-0	38	112.5	F.T.L.
34	31	B	9-0-4-9	36	112.0	F.T.L.
43	25	W	1-0-0-1	40	98.0	F.T.L.
28	38	W	9-0-0-9	40	97.6	F.T.L.
38	15	B	0-0-0-0	40	96.0	F.T.L.
52	33	W	7-0-1-7	40	94.0	F.T.L.
56	23	W	2-0-0-2	40	93.5	F.T.L.
41	38	B	2-0-0-2	34	92.0	F.T.L.
46	36	B	4-0-0-4	37	86.0	F.T.L.
21	25	B	1-1-3-1	28	78.5	F.T.L.
54	32	B	1-0-0-1	22	76.5	F.T.L.
7	42	B	3-0-0-1	40	67.6	F.T.L.
3	32	W	2-0-1-2	30	66.0	F.T.L.
6	30	W	1-0-0-1	39	66.0	F.T.L.
14	40	W	6-0-0-6	36	64.4	F.T.L.
2	17	W	0-0-0-0	38	64.0	F.T.L.
1	17	W	0-0-0-0	30	60.0	F.T.L.
16	22	W	1-0-0-1	39	59.2	F.T.L.
15	20	B	3-0-0-1	39	57.6	F.T.L.
4	17	W	0-0-0-0	34	56.6	F.T.L.

TABLE II. NINETEEN CASES OF CHRONIC NEPHRITIS COMPLICATING PREGNANCY

CASE NO.	AGE	COLOR	PARITY	DURATION OF PREG. WHEN URINE OBT.	F.N.	BABY
39	34	W	2-0-0-2	40	64.0	F.T.L.
42	36	B	8-0-0-6	40	60.0	F.T.L.
53	45	B	7-0-3-6	40	59.5	F.T.L.
62	43	W	15-0-4-12	38	57.2	F.T.L.
31	21	W	0-1-0-0	33	56.0	36L
55	25	W	0-0-0-0	40	55.0	F.T.L.
33	44	W	8-0-2-8	34	54.5	36D
51	19	W	0-1-0-1	34	52.5	37L
12	49	B	4-0-3-3	38	52.4	F.T.L.
30	21	W	0-1-0-0	30	52.0	36L
44	34	B	3-0-0-3	34	51.0	F.T.L.
58	27	B	2-0-1-2	38	51.0	F.T.L.
50	19	W	0-1-0-1	37	49.0	37L
47	37	B	12-0-0-12	32	48.5	32L
32	36	B	7-0-0-6	40	48.0	F.T.L.
26	32	B	3-0-3-3	40	44.0	F.T.L.
13	36	W	8-0-0-8	39	44.0	F.T.L.
59	39	B	4-0-0-5	38	43.2	F.T.L.
17	42	B	10-0-0-10	40	40.0	F.T.L.

These results also agree with the conception that premature babies are common in chronic nephritis complicating pregnancy.

No attempt was made to subdivide these patients into those who had suffered from chronic nephritis prior to the first pregnancy, or those developing chronic nephritis during the course of subsequent repeated pregnancies, or to differentiate between the types of chronic nephritis.

Smith and Smith^{9, 10} obtained normal estrin levels in several patients who were definitely "nephritic." Our experience, on the other hand, has shown definite lowering of the level of estrin excretion in cases of chronic nephritis complicating pregnancy.

While chronic nephritis complicating pregnancy is not generally considered a true toxemia, we feel that the significant lowering of estrin excretion as found in our series of cases is worthy of mention, since it apparently has not been recorded elsewhere.

PREECLAMPSIA

The 20 cases of preeclampsia are shown in Table III. They were characterized by sudden elevation of blood pressure, sudden appearance of albumin in urine previously normal, increased uric acid retention in the blood, and by the sudden onset of subjective symptoms in late pregnancy varying from edema of the feet and ankles to edema of the face and hands, abnormal weight gain, nausea and vomiting, headache, precordial pain, and visual disturbances. All these patients were admitted

TABLE V. SHOWING EXCURSION AND OVERLAPPING OF F.N. IN THE THREE GROUPS OF CASES SUMMARIZED IN TABLES I TO III

F.N.		
152.0		
↓		
76.0		
67.6		
66.0		Normal group
66.0		
64.4		
64.0	64.0	
60.0	60.0	
59.2	59.5	
57.6	57.2	
56.6	56.0	
	55.0	
	54.5	
	52.5	
	52.4	Chronic nephritis com-
	52.0	plicating pregnancy
	51.0	
	51.0	
	49.0	
	48.5	
	48.0	
45.5	44.0	
44.5	44.0	
42.0	43.2	
40.5	40.0	
40.0		
39.0		
38.5		
38.5		Preeclampsia
38.0		
↑		
28.5		

NORMAL CASES

The 21 cases shown in Table I were all normal in the sense that they were not suffering from any of the late toxemias of pregnancy which could be discovered clinically, and were admitted to the hospital mainly for convenience near term for the induction of labor. Seven were admitted because of the following complications:

Ischiorectal abscess
Thrombophlebitis
Pulmonary tuberculosis
Rheumatic heart disease
Cephalopelvic disproportion, 2 cases
Salpingitis

Six of these patients were primigravidas and 15 were multigravidas; 13 were white and 8 were colored.

The average duration of pregnancy at the time the twenty-four-hour specimens were obtained was thirty-six weeks. The average "ferric chloride number" (F.N.) was 83.3, the highest being 152.0 and the lowest 56.6 (Table IV). Such a wide variation in this finding cannot be explained on the basis of the duration of pregnancy because with the exception of Case 54 (Table I) in which the duration of pregnancy was twenty-two weeks, the patients were from twenty-eight to forty weeks pregnant. Possible explanations of this wide variation are: first, individual variations in the amount of estrin excreted; and second, certain of these normal patients might have been on the verge of some toxemia which had not manifested itself clinically, but was accompanied by a lowered estrin excretion. This second idea is in keeping with the findings of Smith and Smith^{9,10} who observed that several of their patients did not develop clinical symptoms of toxemia until some time after a decrease in urinary estrin was noted. This, of course, suggests the possible prognostic value of periodic determinations of estrin excretion throughout pregnancy. Such routine determinations for all the patients registered in the prenatal clinic would not be possible at present.

All patients in the normal series were delivered of full-term living children who survived the neonatal period.

CHRONIC NEPHRITIS COMPLICATING PREGNANCY

Table II represents a series of 19 cases of chronic nephritis complicating pregnancy, characterized by nitrogen retention in the blood, edema, albuminuria, and elevated blood pressure which failed to return to normal levels after delivery. One patient (Case 47, Table II) died following the interruption of her pregnancy because of severe chronic nephritis. This was the only maternal death in 60 cases or 1.6 per cent. All these patients were admitted to the hospital because of evidences of toxemia. There is but one primigravida in this series which is in keeping with the observation that chronic nephritis complicating pregnancy affects multigravidas more frequently than primigravidas. Many of these patients had symptoms of toxicity for from two to six months prior to delivery. Nine patients were white and 10 were colored.

The average duration of pregnancy at the time of collection of the twenty-four-hour urine was 37.1 weeks, while the average "ferric chloride number" (F.N.) was 51.67, the highest, 64.0, and the lowest, 40.0 (Table IV). The wide variation seen in the normal group was not found in this group.

In this series there were 13 full-term living children, a thirty-six-week stillborn baby, two each of thirty-six- and thirty-seven-week babies who survived the neonatal period, and one thirty-two-week living baby who survived the neonatal period.

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LOMBARD AND GREENE STREETS

THE BORDERLINE PELVIS

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ON SEVERAL occasions¹ I have made the bold inference that Smellie's theory of determining the length of the true conjugate diameter by subtracting 1.5 to 2 cm. from the diagonal, was not tenable. These statements had been based upon observation of occasional cases. In this communication I shall present facts and figures from my own systematic study of a series of cases, which are somewhat enlightening, especially in reference to what may be termed "the borderline pelvis." To my mind, "borderline pelvis" is as arbitrary a term as "test of labor." Textbooks give a specific definition, based upon the commonly practiced method of Smellie, the application of which frequently results in an inadequate test of labor and cesarean section, as well as an inaccurate understanding of the frequency and possibility of delivery through the natural route. The manner of handling the woman with a normal pelvis or the one with an absolutely contracted pelvis gives us little concern, and in such cases obstetric opinion does not vary. The class that falls in between these two limits requires the best obstetric judgment; and it is here that opinions vary.

My own conception of a borderline pelvis is one in which, disregarding a rigid perineum, the sacral promontory may be readily reached. This method eliminates the necessity of placing borderline pelvises into various groups with stated indications for treatment of each group. For I shall attempt to show that heretofore the vast majority of these cases have been improperly classified and subjected to the danger of radical procedures. In this paper I am concerned with the size of the pelvic inlet and not with classical means of grouping pelvises such as the excellent one proposed by Caldwell, Moloy, and D'Esopo.² It is pleasing to note that Fitzgibbon³ does not consider it possible to classify contracted pelvises so as to lay down the treatment of cases in groups. Although he believes that the degree of contraction greatly influences the prognosis of the case, it does not exclude pelvic delivery in the major degrees, nor assure pelvic delivery in the minor degrees. Peckham and Kuder⁴ in discussing labor in contracted pelvises wisely avoid confusion by regarding

to the hospital because of toxemia. In keeping with the observation that primigravidas are more prone to preeclampsia, we see that all but one patient in this series fall into this classification. Nine patients were white, 11 were colored. The average duration of pregnancy when the twenty-four-hour urine specimens were obtained was 38.1 weeks, while the average "ferric chloride number" (F.N.) was 36.87, the highest 45.5, and the lowest, 28.5 (Table IV).

The pregnancies of the patients in this group terminated in the births of full-term living infants, with the exception of thirty-four-week and thirty-seven-week living premature babies who died in the neonatal period.

In this series we have confirmed the work of Smith and Smith⁸⁻¹¹ in finding a definitely lowered level of estrin excretion in preeclampsia (see Tables IV and V).

In Table V the excursion and overlapping of estrin excretion in the three groups of cases are given. In 18 cases, or 30 per cent, there is overlapping, but in 42, or 70 per cent, of the cases the results seem to be of value in differential diagnosis. Given "ferric chloride numbers" of 83.3, 51.67 and 36.87 (Table IV), perhaps we would be justified in classifying the respective patients as normal, those suffering from chronic nephritis complicating pregnancy, and preeclamptic.

SUMMARY

1. By means of a chemical test for pregnancy⁶ a definitely lowered level of estrin excretion in the urine has been found in a series of cases in the late toxemias of pregnancy. Determinations upon the urines of normal patients in the last trimester of pregnancy were run concurrently as controls to establish a normal level.

2. In this series preeclampsia was not subdivided into "low reserve kidney" and preeclampsia. The late toxemias of pregnancy are considered in this paper as: chronic nephritis complicating pregnancy, preeclampsia, and eclampsia. No cases of true eclampsia appear in this series.

3. Sixty hospitalized patients in the last trimester of their pregnancies were carefully studied clinically, and complete twenty-four-hour urine specimens were examined for estrin.

4. While the line of demarcation is not sharp in 30 per cent of the cases, it has been possible to divide 70 per cent into those normal patients who were free from any evidences of toxemia; those patients suffering from chronic nephritis complicating pregnancy; and those whose clinical diagnosis was preeclampsia. The average estrin excretion expressed as the "ferric chloride number" for 21 normal cases was 83.30; for 19 cases of chronic nephritis complicating pregnancy, 51.67; and for 20 cases of preeclampsia, 36.87.

The authors wish to express their sincere appreciation to M. J. Schmulovitz for invaluable technical assistance and advice, and for his translations of some of the references; to Dr. L. H. Douglass for his review of this paper; and to the resident and nursing staffs of the Obstetrical Service in the University Hospital for their indispensable aid in obtaining the necessary specimens.

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abling a check on all calculations. All examinations, calculations and roentgen interpretations were personally conducted, in order to eliminate, as far as possible, any source of error.

Williams⁶ states: "Were we able to measure satisfactorily the angle formed between the symphysis and conjugata diagonalis, the exact length of the true conjugate could be ascertained." This is the procedure followed in the use of the inclinometer,^{1, 6} where the height of the symphysis, the length of the diagonal conjugate and the size of the angle between them is noted. The calculator incorporated in the instrument enables accurate determination of the true conjugate diameter.

Reference has already been made to the fact that the inclinations of the symphysis and of the diagonal conjugate vary in all women.⁸ Since it is these two angles that determine the size of the obstetric angle (which is that contained between the symphysis and diagonal

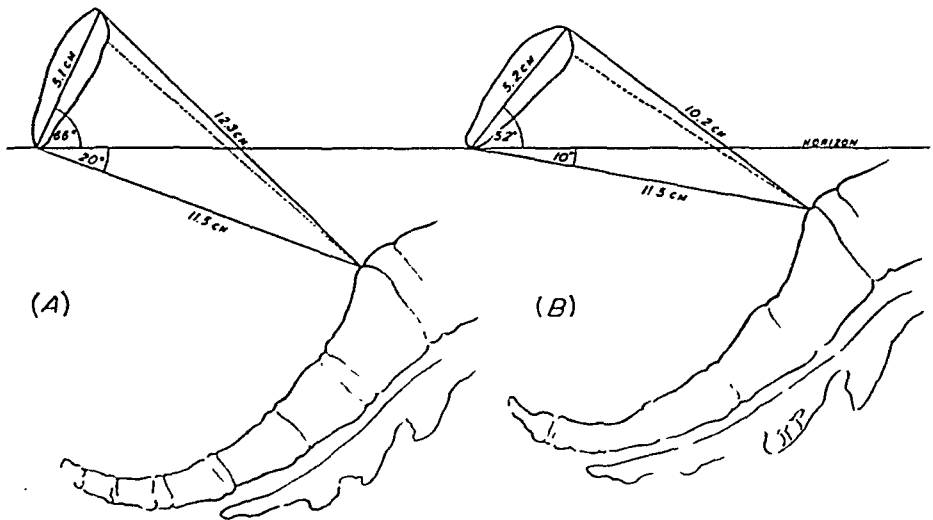


Fig. 2.—Two pelvises taken from the author's series. Although the diagonal conjugate diameters are equal, the true conjugate in (A) measures 12.3 cm. and in (B) 10.2 cm. Patient (a) delivered a 7 pound 14 ounce baby after a five-hour labor. Patient (b) was delivered of a 7 pound 7 ounce baby by cesarean section.

conjugate), it is readily understood that the size of the true conjugate cannot be determined by the length of the diagonal conjugate per se; and that seldom do we find two pelvises with identical diagonal conjugates in which the true conjugates are equal (Fig. 2). In all pelvises likewise, the inclination of the inlet varies, a factor that frequently is concerned with engagement regardless of pelvic dimensions.

It may be briefly stated that with a given diagonal conjugate a more favorable inclination of the symphysis causes a shortening of the true conjugate and vice versa (Fig. 2).

Since the factors that enter into the determination of the size of the true conjugate diameter are altered by changes in posture, postural changes warrant some consideration, as they may seriously affect the prognosis in a borderline pelvis. Although all textbooks make the statement that flexion of the thighs on the abdomen diminishes the true con-

a pelvis as contracted if the diagonal conjugate measures 11.5 cm. or less. Maxwell⁵ selects the length of the diagonal conjugate rather than the estimated true conjugate as the determining measure, because the former is an actual measurement. Thus, modern authors are beginning to realize that little dependence may be placed upon the method of *estimating* the length of the true conjugate from the diagonal.

Patients with pelves of normal contour, in whom the sacral promontory could be reached without difficulty, were selected from the prenatal clinics of Georgetown University, Garfield Memorial, Gallinger Municipal, and Columbia Hospitals. Although hundreds of patients had been examined, a complete study of the bony pelvis in a definite routine manner was made in eighty women. All measurements were

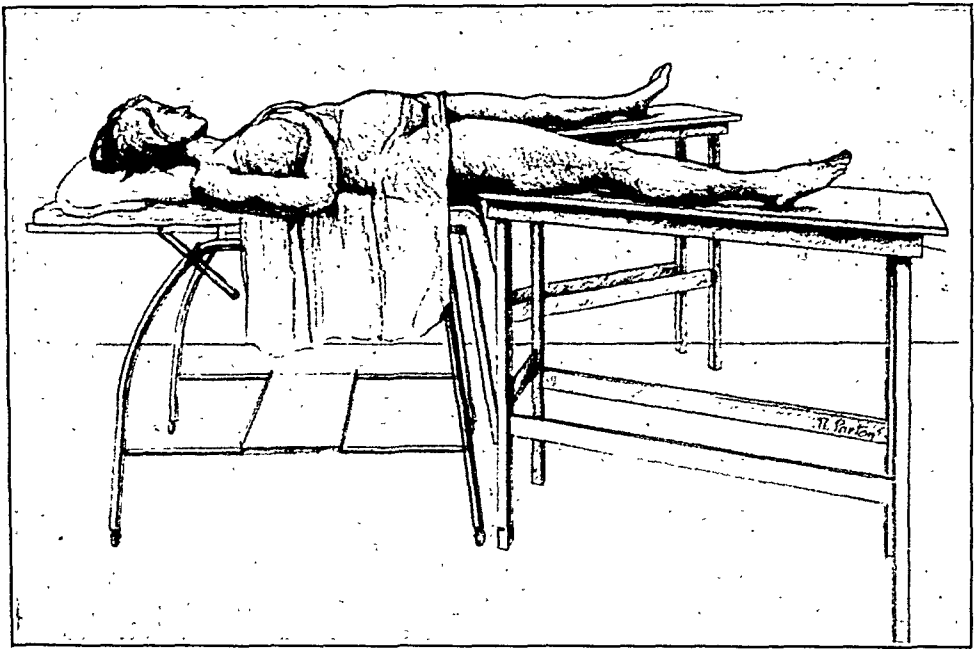


Fig. 1.—Patient recumbent for internal pelvimetry and anteroposterior roentgenography. Examiner stands between tables.

made with the obstetric inclinometer and it was necessary to select patients who would cooperate and lie perfectly quiet, for in using this instrument the pelvis must remain in a fixed position until all the necessary readings are taken. The patient is placed in the recumbent posture with legs extended and separated, being supported on two tables (Fig. 1). It is difficult to examine in this position, and unusual cooperation is required on the part of the patient. Yet it was necessitated by the fact that x-ray studies were made in the majority of these cases to confirm the calculations of the conjugata vera. Since variation in posture causes alteration in length of the true conjugate, it was necessary to examine patients in the same attitude (recumbent posture) in which they were placed for roentgenographic pelvimetry, thus en-

whether it is possible to increase the size of the inlet by postural change, since observations of this type had never been made on living subjects. Although I have proof of the variation in size of the pelvic inlet, I have never advocated the use of the Walcher position. Besides being an uncomfortable attitude for a woman to assume during labor, the availability for engagement of the important pelvic planes is diminished. For when the thighs are allowed to hang over the edge of the table, an inlet that does not have a favorable inclination ordinarily becomes worse. The inclination of the symphysis likewise assumes a vertical attitude, making it necessary for a head to take a downward course in order to get beneath it, even if it succeeds in entering the brim. In addition the abdominal muscles are put under great tension and stretched over the in-

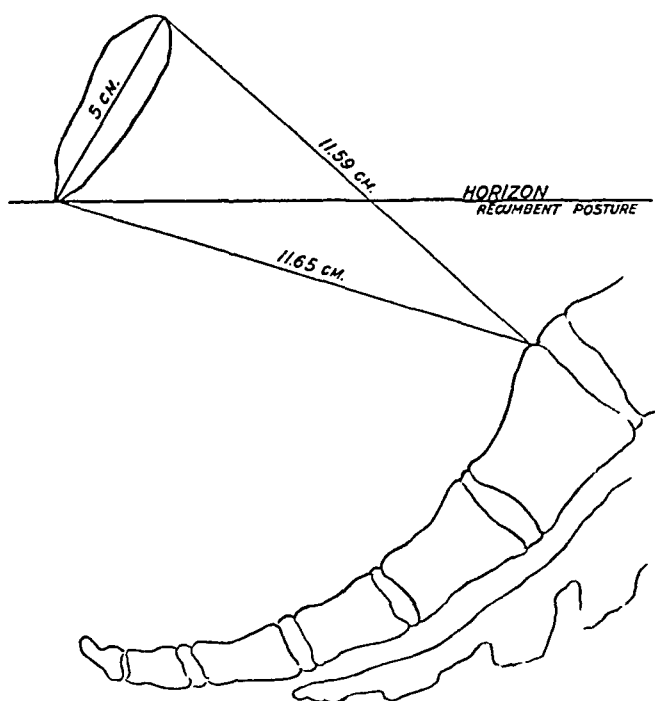


Fig. 4.—Pelvigram of the average pelvis in this series, with patient in recumbent posture. It will be recalled that in the ordinary modified lithotomy position in which women are usually measured, all diameters are somewhat smaller.

let, which is assuming a parallel position to the horizon, thus limiting the space over the inlet for engagement of the presenting part. Were the direction of the forces of expulsion correspondingly altered, so as to approach the axis of the superior strait, engagement would be facilitated. But what actually happens is a limitation of the motion of the uterus by the tense abdominal wall, so that the fundus cannot rise at the height of a contraction in an effort to bring the expulsive force in line with the axis of the superior strait, but is directed almost parallel with the inlet and more or less perpendicular to the symphysis. In a pelvis that has an unusually good inclination the Walcher position may not hinder engagement and be of some benefit by enlarging the inlet. In cases of moderately favorable or those of faulty inclination, the Walcher posi-

jugate diameter and that hyperextension (as in Walcher position) causes increase in its length, no investigations had been conducted on living subjects to either prove or disprove these contentions, until those made by me a few years ago. Placing a patient in the lithotomy position causes shortening of the diagonal conjugate diameter, with increase in its inclination, a reduction in the inclination of the symphysis and a resulting shortening of the true conjugate diameter. The diminution in size of the true conjugate is usually between 0.5 and 1 cm., but

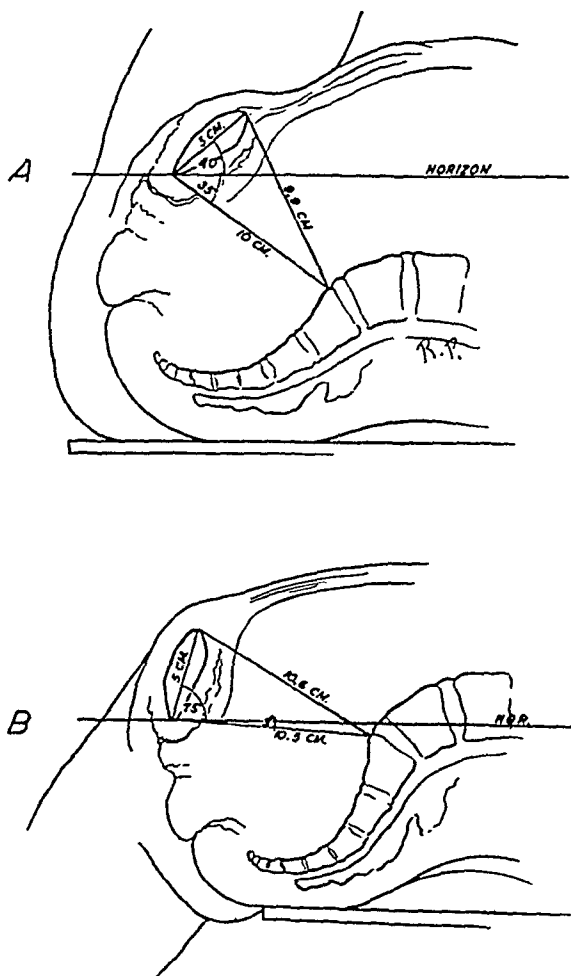


Fig. 3.—A, Patient in lithotomy position. B, Same patient in Walcher position. The factors responsible for alterations in length of pelvic diameters are shown. Note how, in the Walcher position, the tense abdominal muscles limit area over inlet and also prevent the rise of the fundus to its normal elevation at the height of a contraction; factors interfering with engagement.

varies in different subjects. In the Walcher position (Fig. 3), I have found an increase in the true conjugate, varying from 0.3 cm. to over 1 cm. This is effected by an increase in the length of the diagonal conjugate, and an increase in the angle of inclination of the symphysis; in this case, of course, inclination of the diagonal conjugate is diminished.

Since the Walcher position causes an increase in the conjugata vera and diagonalis, why has it not held a more popular place in the management of borderline cases? Possibly some obstetricians have doubted

receive a sufficient test of labor; abdominal operation could have been avoided, but that operator believes in a six-hour test of labor. There were no cases of true conjugate actually measuring less than 9 cm. in this series, showing that such pelves are extremely rare. These figures are consistent with the views of Fitzgibbon³ who states that 70 to 80 per cent of patients with borderline pelves deliver normally.

The smallest pelvis that permitted delivery of the largest baby (9 pounds 6 ounces) from below, was one with a calculated true conjugate of 9.1 cm. or an available true conjugate of about 8.5 cm. Labor lasted fifteen hours. The largest pelvis that required cesarean section after a suitable test of labor had an available true conjugate of 11 cm., the baby weighing 9 pounds 2½ ounces. Such occurrences, although uncommon, are in accord with the view of Fitzgibbon³ who stated that the amount of contraction does not always exclude pelvic delivery even in the major degrees, nor assure pelvic delivery in the minor degrees.

I naturally conclude that in the average patient the true conjugate diameter measures more than 11 cm. and that the difference between the true and the diagonal conjugate is less than 1.5 cm. This fact should persuade us to be more generous with the test of labor. It emphasizes also that one is not justified in placing a pelvis in the borderline or contracted group, merely because of a true conjugate diameter that has been estimated from the diagonal conjugate by the usual means advocated by Smellie. Most women with borderline pelves deliver through the natural channel and usually spontaneously, because the true conjugate is actually larger than we have been accustomed to estimate.

TABLE II. ACCORDING TO SMELLIE'S METHOD, THE SAME SERIES OF PATIENTS, IF EXAMINED IN MODIFIED LITHOTOMY POSITION, WOULD BE IMPROPERLY GROUPED

TRUE CONJUGATES	NORMAL DELIVERY	LOW FORCEPS	MID- FORCEPS	CESAREAN SECTION (ALL FOR DISPRO- PORTION)	TOTAL
11.5 to 10.5 cm.	8	0	0	0	8
10.4 to 9.5 cm.	30	7	0	4	41
9.4 to 8.5 cm.	20	2	2	3	27
8.4 to 7.5 cm.	2	0	0	2	4
Total	60	9	2	9	80

By Smellie's method in the usual modified lithotomy position, there would be no patients with a true conjugate over 11.5 cm., and this has been the general concept. Forty-one patients would be classed as having a true conjugate of 10.4 to 9.5 cm., and of these 4 had cesarean sections and 7 low forceps. Twenty-seven patients would be regarded as having a true conjugate of between 8.5 and 9.4 cm., and as such would probably have received a very short and inadequate test of labor, and more than 3 cesarean sections might have been performed in this group. All 4 patients with a true conjugate between 7.5 and 8.4 cm., under

tion would be a disadvantage, for any increase in the size of the inlet is of no value, since the inclination of the plane of the inlet is such as to limit or even preclude its availability. It seems that the hanging leg position during labor may have a place only in borderline pelvises of unusually good inclination.

As previously stated, until recently the nearest approach to the measurement of the conjugata vera has been the deduction of 1.5 cm. to 2 cm. from the diagonal conjugate. With the aid of the inclinometer I have been able to *calculate* the length of the true conjugate with precision and check these determinations by both anteroposterior and lateral pelvimetric roentgenography and in some cases by direct measurement of the inlet at cesarean section. In the series of 80 cases the average diagonal conjugate was 11.65 cm. The average true conjugate was 11.59 cm. (Fig. 4). In 8 per cent of cases did the customary rule of subtracting 1.5 cm. to 2 cm. from the diagonal conjugate to obtain the true conjugate apply. In 89.5 per cent of the cases the difference was less than 1.5 cm. In 48.7 per cent of cases the true conjugate was either as large or larger than the diagonal conjugate. As judged by the length of the diagonal conjugate and the ability to feel the sacral promontory, my series represents a class of moderately contracted pelvises. Yet within this group we find a preponderance of true conjugate diameters that measure more than 11 cm. Note the large proportion of cases in which there is a small variation in the length of these two diameters. The true conjugate exceeded the diagonal in 37 cases; the size of the *obstetric angle*, which heretofore had been unmeasured, accounts for this.

TABLE I. ANALYSIS OF EIGHTY BORDERLINE PELVES IN RECUMBENT POSTURE, SHOWING ACTUAL CALCULATED TRUE CONJUGATE DIAMETERS AND METHODS OF TREATMENT

TRUE CONJUGATES	NORMAL DELIVERY	LOW FORCEPS	MID- FORCEPS	CESAREAN SECTION (ALL FOR DISPRO- PORTION)	TOTAL
13 to 12 cm.	19	6	0	1	26
11.9 to 11 cm.	27	4	1	1	33
10.9 to 10 cm.	10	0	1	6	17
9.9 to 9 cm.	3	0	0	1	4
8.9 to 8 cm.	0	0	0	0	0
Total	59	10	2	9	80

In this series 59 patients had true conjugates of over 11 cm.; yet I have reason to consider them borderline cases, for if measured in the modified lithotomy position the diagonal conjugates would be 11.5 cm. or less. In this class there were 46 normal deliveries, 10 low forceps, 1 midforceps, and 2 cesarean sections. Between 10 and 10.9 cm., 6 cesarean sections were done in 17 cases; there was one maternal death due to infection following section. This patient, in my opinion, did not

a chance of delivering from below, especially where the fetal skull is not large and the diagonal conjugate is nearer to 10.5 cm.

With a true conjugate diameter of 9 cm. as calculated with the inclinometer, experience shows that a full-term baby of average weight will very seldom deliver spontaneously, for reduction in the size of the biparietal diameter may be limited. Where the true conjugate diameter really measures 8.5 cm. or 8 cm. or less, delivery of a living full-term child through the birth canal is hardly possible. For we must further deduct from such a diameter 0.7 cm. to reduce the true conjugate diameter to the obstetric, or better term is the available conjugate.

In my series there were two fetal deaths. Both fetuses died of intracranial hemorrhage; one weighing 6 pounds 14 ounces followed Scanlon maneuver in a pelvis with an available conjugate of 10.7 cm.; the other followed normal delivery in a pelvis having an available conjugate of 12 cm.

Regarding the prognosis for the fetus in borderline and contracted pelves, Williams⁶ quotes as examples figures from Michaelis, Litzmann and Schwartz, giving the mortality prior to 1865, when cesarean sections were seldom performed.

CONJUGATA VERA	FETAL MORTALITY
1. 9.25 to 8.5 cm.	5%
2. 8.4 to 7.5 cm.	16.9%
3. 7.4 to 7.0 cm.	52.9%

From my study it may be safely assumed that these rates are too exceedingly low to be correct, and may be accounted for by reference to my remarks, that the conjugata vera in these cases had been estimated from the diagonal. That in reality direct mensuration, had it been possible, would have revealed pelves much larger than stated in the above table. It should be recalled that from the above tabulated measurements, 0.7 cm. must be deducted to obtain the "available true conjugate." Therefore I disagree entirely, and safely conclude that for pelves as stated in Class 1 the fetal mortality is and should be much greater. In Class 2, engagement of a normal size head is almost always impossible. In Class 3, engagement of a normal size head is always impossible.

These statements are not made to encourage the performance of cesarean section, but, on the contrary, to call to the attention of the obstetrician the fact that he often is dealing with a larger pelvis than he surmises, and that in borderline cases there is usually a good chance of his patient delivering from below. It may be said without hesitation that pelves actually measuring 8.5 cm. or less in the true conjugate are not ample for safe delivery of a child of normal size. I should call these absolutely contracted pelves. Then the lower limit of borderline pelves would be about 9 cm. for the true conjugate, or 8.3 cm. for the available conjugate, for we deduct 0.7 cm. as being the

ordinary circumstances might have been sectioned, instead of just two.

The smallest pelvis that I have ever encountered was one that had a calculated true conjugate of 8 cm. (Fig. 5). I have never before or since seen one that actually measured less; and that covers examinations of several thousand women. According to Table II such pelvises are erroneously believed to be common; in this table there appears to be a frequency of 5 per cent.

Ample reason has been given why a diagnosis of borderline pelvis should not be made from true conjugates that are estimated from the diagonal by subtracting 1.5 cm. to 2 cm. This method in actual practice affords a distorted prognosis, in view of the figures presented. Williams⁵ like most authorities regards a pelvis with an estimated conju-

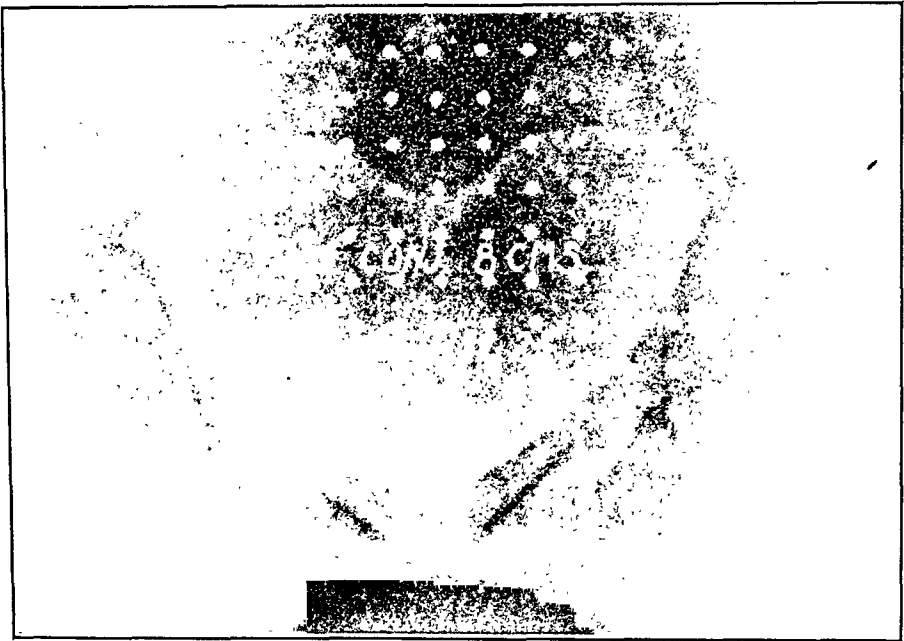


Fig. 5.—A-P roentgenogram of smallest pelvis encountered in the various clinics, showing that pelvises customarily classified as absolutely contracted are extremely rare. (The middle of the upper border of the symphysis is designated by the heavy line.)

gata vera of 9 to 10 cm. as being in the mild borderline class and says that spontaneous delivery with a full-term baby of normal size and with normal expulsive forces is the rule. In this class he refers to pelvises with a diagonal conjugate varying between 12 and 10.5 cm. The vast majority of these should and do deliver normally, because the true conjugate in 89 per cent of them is much larger than 9 to 10 cm. And in borderline pelvises of the more severe type, that is, presumed to be between 9 and 7.5 cm. and estimated from diagonal conjugates varying between 10.5 and 9 cm., he says the greatest difficulty is experienced in predicting the course of labor and in laying down rules of treatment. I feel that in cases in this type, since the true conjugate frequently equals or may surpass the length of the diagonal conjugate, some patients should stand

EXTRAPERITONEAL (LATZKO) CESAREAN SECTION*

WITH A REPORT OF CASES AND SUGGESTED MODIFICATIONS IN TECHNIC

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ACCUMULATED experience with the extraperitoneal (Latzko) cesarean section, in various obstetric clinics throughout the country, is gradually serving to establish it as an invaluable means of delivery for selected cases.

The purposes of this paper are:

1. To discuss the indications for extraperitoneal cesarean section and to emphasize its advantages as a means of delivery when indicated.
2. To describe a point in technic which during dissection should reduce the danger of bladder injury.
3. To present a modification in technic whereby the Latzko procedure is made adaptable for the suprapubic delivery of a patient regardless of whether or not the cervix is dilated and retracted.
4. To demonstrate a method for more adequate drainage of the space of Retzius following delivery by the Latzko procedure.
5. To report a small series of patients delivered by this method at the Woman's Hospital.

It is my opinion that indications for extraperitoneal cesarean section arise in two classes of infected or potentially infected cases as follows:

1. Cases in which, through faulty judgment, it is eventually found in the course of labor that, because of bony dystocia, vaginal delivery of a living child is impossible or extremely problematical. Delivery by extraperitoneal cesarean section has been successfully accomplished in such cases after attempted operative delivery by vagina.
2. Cases in which, in spite of prolonged first-stage labor, the cervix has failed to dilate. This group of cases includes those which have true cervical dystocia and those in which the cervix has failed to dilate as the result of primary uterine inertia.

When, in the best interests of the mother or child, delivery of such patients becomes necessary, we are frequently faced with possible uterine infection which has been favored by early rupture of membranes, the contamination of repeated vaginal examinations and a mother whose vitality and resistance have been reduced by the conditions resulting from prolonged first-stage labor. Such patients also frequently have borderline pelvises, usually of the male type, and large babies showing signs of fetal distress.

*Read at a meeting of the New York Obstetrical Society, October 13, 1936.

distance from the middle of the thickness of the pubic symphysis to the posterior surface. Therefore, were it possible to classify contracted pelves by direct measurement of the conjugata vera, we would find that most pelves that are now placed in the borderline class would permit spontaneous delivery, for they are larger than estimated. We would be surprised to find that the average pelvis is larger than we believe it to be. Also the upper limit of the absolutely contracted class should be raised, so as to include larger true conjugates. Pelves of the absolutely contracted type as determined by Smellie's method (that is, with a true conjugate of 7.5 cm. or less) are very uncommon.

SUMMARY

In the series presented there were 59 normal deliveries, 10 low forceps, 2 midforceps and 9 cesarean sections. The one maternal death could have been avoided, for it resulted from cesarean section following inadequate test of labor. Only 2 infants were lost; both deaths were due to intracranial hemorrhage.

CONCLUSIONS

1. Definite rules concerning the formerly accepted classifications and treatment of contracted pelves are not tenable.

2. When the sacral promontory is readily palpated, the pelvis should be classed as borderline.

3. In the series presented, all measurements were made in the recumbent posture; if examined in the usual modified lithotomy position, the internal measurements of these pelves would have been somewhat smaller.

4. The outcome in a borderline pelvis is not only governed by size of the "available true conjugate diameter," but also by the inclination of the inlet.

5. The value of the Walcher position is not strongly endorsed.

6. Proper recognition of borderline pelves from the length of diagonal conjugates with disregard to Smellie's rule of subtracting 1.5 to 2 cm., will result in better tests of labor and fewer cesarean sections. In only 8 per cent of cases does Smellie's rule apply.

7. The mere application of Leopold's fourth maneuver is of greater prognostic value in borderline cases than grouping pelves according to true conjugates which were estimated by Smellie's method.

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One of the greatest objections to the Latzko operation has been the danger of bladder injury, during dissection, to expose the anterior surface of the lower uterine segment. In Steele's² series of 59 cases this accident occurred six times. In our own series of 27 cases the bladder was accidentally opened once.

A study of the anatomic structures around the bladder (Fig. 1, *A*) shows that its musculature is completely surrounded by a thin but definite layer of endo-

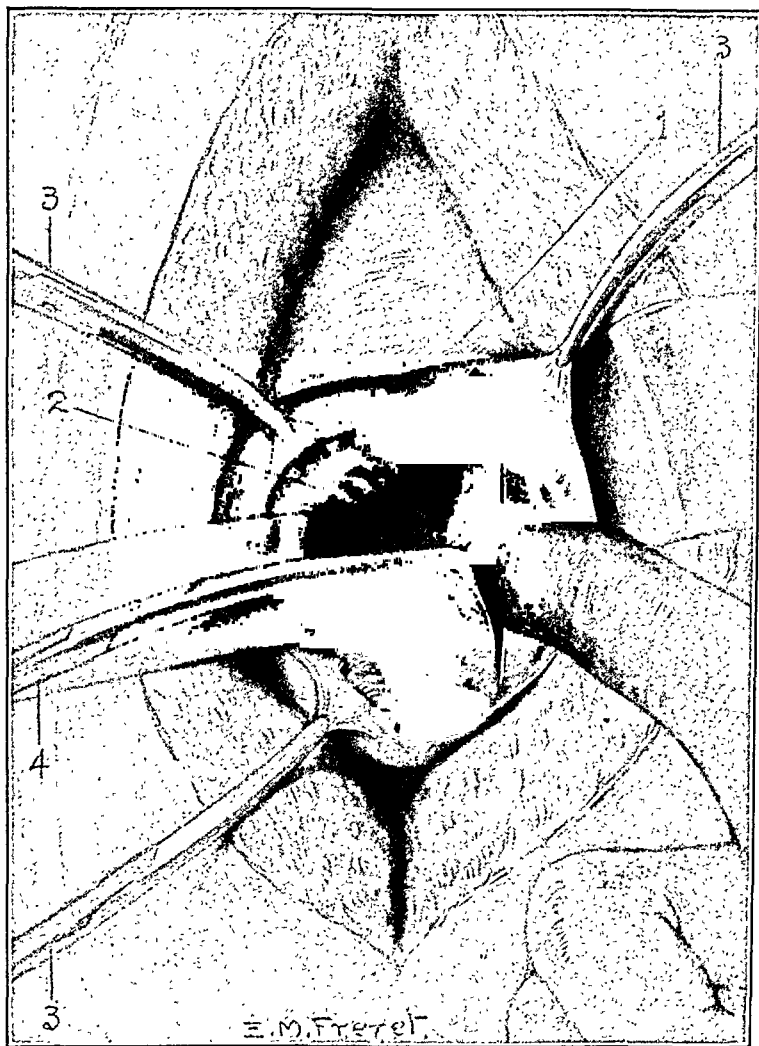


Fig. 2.—Diagram showing bladder displaced laterally and endopelvic fascial capsule about bladder. 1, Uterovesical fold of peritoneum. 2, Bladder. 3, Clamps on incised endopelvic fascia on anterior surface of bladder. 4, Clamps on incised endopelvic fascia on posterior surface of bladder. Blunt dissection is continued behind this layer rather than within the endopelvic fascial capsule of the bladder.

pelvic fascia (Fig. 1, *A*, 1). After incising the abdominal wall the first step in dissection is to open the layer of endopelvic fascia (1), covering the anterior surface of the distended bladder by a longitudinal incision in the midline. After this layer has been incised, the bladder can easily be displaced, from within its endopelvic fascial capsule¹ on the left side (*B*), by blunt dissection. As soon as the anterior surface of the lower uterine segment is reached (Fig. 1, *B* and Fig. 2), the layer of endopelvic fascia on the posterior surface of the bladder can readily be seen as a

Experienced obstetricians are familiar with the difficulties and dangers which attend vaginal delivery, before full cervical dilatation has been reached. As a rule, it involves:

1. Manual dilatation of the cervix or multiple (Dührssen's) incisions.
2. A difficult operative delivery which occasionally either necessarily sacrifices the life of the infant or leaves the infant with some degree of physical handicap, the result of birth injury.
3. An immediate risk to the mother from trauma, hemorrhage, shock, and infection, and finally the possibility of some degree of permanent physical handicap from unavoidable vaginal or uterine birth injuries, which may be difficult to repair.

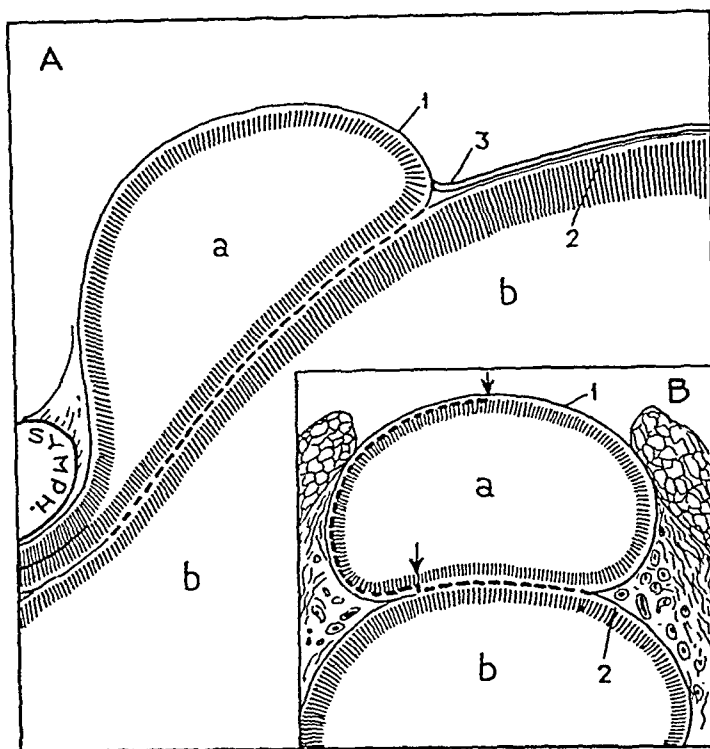


Fig. 1.—Diagram showing anatomic relationships of bladder and anterior uterine wall in A, the sagittal plane and in B, cross-section. *a*, Bladder. *b*, Uterine cavity. 1, Endopelvic fascia completely surrounding the bladder musculature. 2, Endopelvic fascia surrounding the musculature of the uterus. 3, Uterovesical fold or peritoneum. The dotted line, between the layers of endopelvic fascia covering the bladder and lower uterine segment, shows the proper plane of cleavage in which dissection can be readily and safely carried out. It is the space which is opened in the so-called "low flap" cesarean section. In B, the arrows indicate the points at which the endopelvic fascia about the bladder is opened during the dissection. It will be noted that as soon as the anterior uterine segment is reached, the endopelvic fascia on the posterior surface of the bladder is opened and dissection is continued between this layer and a similar layer on the uterine musculature.

Those interested in an historical review of the technical development of extraperitoneal cesarean section and a complete description of the details of the Latzko technic are referred to articles by DeLee,¹ Steele,² and Burns.³ It is the purpose of this paper to suggest three additional points in technic, not previously described, which it is believed, in certain cases, may facilitate the performance of the procedure and contribute to its safety.

the peritoneum are carefully brought into apposition, as shown in Fig. 4, before the uterine cavity is opened. This procedure not only gives room for delivery in cases where it is difficult or impossible to get adequate exposure of the lower uterine segment, but makes the procedure available as a means of delivery regardless of the degree of cervical dilatation or retraction.

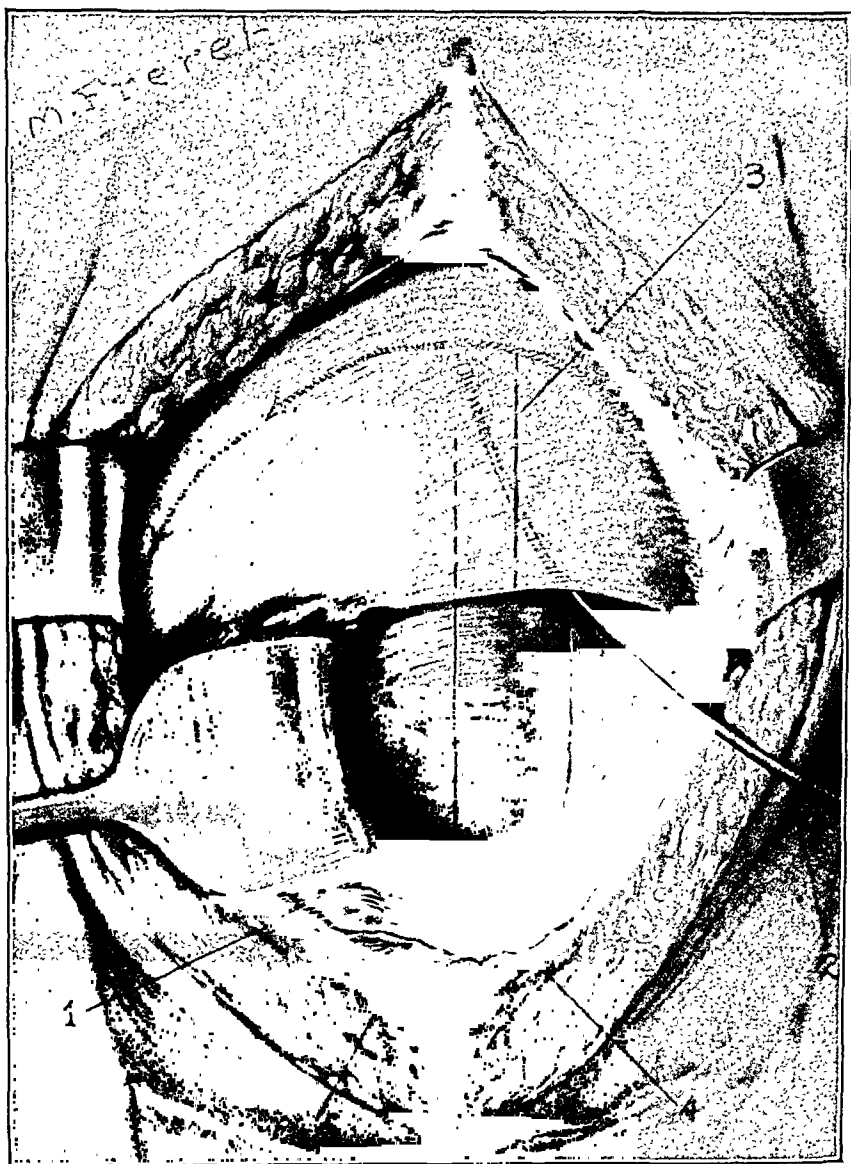


Fig. 3.—1, Retracted bladder. 2, Probe under dissected tense uterovesical fold of peritoneum. 3, Line of incision through uterovesical fold of peritoneum. 4, Line of incision in lower uterine segment.

It is admitted that deliberate opening of the peritoneal cavity, as described, is a violation of the principle of extraperitoneal cesarean section. However, the incised peritoneum can be securely closed by careful suturing so that subsequent contamination of the peritoneal cavity through the suture line must be slight, if any. This step in technic has been successfully used in four frankly infected cases.

smooth glistening layer. It has been found that this layer can be immediately opened and dissection can more readily be continued behind the layer (Fig. 1, *B* and Fig. 2), rather than making further attempt to free the bladder from its fascial capsule. When dissection is continued between this layer (Fig. 1, *B*, 1), and a similar layer (Fig. 1, *B*, 2) covering the musculature of the lower uterine segment, it will be found that a free, practically bloodless, space has been entered and that the anterior surface of the lower uterine segment can readily be exposed. Between these fascial planes (Fig. 1, 1 and 2) the dissection can easily be carried laterally or upward behind the uterovesical fold of peritoneum (Fig. 1, 3), far beyond the upper border of the bladder. This is exactly the same almost bloodless space which is entered in displacing the bladder downward in doing the so-called "low flap" cesarean section by the abdominal route.

It is believed that bladder injury usually occurs when, in order to get adequate exposure of the lower uterine segment, persistent efforts are made to continue the dissection posteriorly within its fascial capsule.

Another serious criticism of the Latzko operation has been the fact that the uterovesical fold of peritoneum is too frequently opened during the operative dissection or while extracting the infant. If the injury occurs before the uterine cavity is opened, it can be immediately repaired to prevent later contamination of the peritoneal cavity. However, if the peritoneal cavity is accidentally opened during extraction of the infant, contamination of the peritoneum is bound to occur, thereby defeating the purpose of the procedure.

Previous writers on this subject have invariably claimed that the procedure, as a means of suprapubic delivery, is inadvisable unless the cervix is at or near full dilatation. The advantages are that when cervical dilatation is well advanced, and the cervix is at least partially retracted, the lower uterine segment increases in length; the uterovesical fold of peritoneum is elevated, and the uterine vessels and ureters are laterally displaced. These physiologic changes in relationship of the structures, for obvious reasons, greatly facilitate the procedure.

In our experience, indications for extraperitoneal cesarean section occasionally arise in obese women with male pelves and large babies, in whom adequate exposure of the lower uterine segment is difficult, even though these changes have occurred. Furthermore, in our experience the most frequent indication for extraperitoneal section occurs in women in whom, in spite of prolonged first-stage labor, the cervix has failed to dilate more than 3 to 5 cm., because of true cervical dystocia, or uterine inertia or both. In spite of careful dissection, in either of these types of cases, it is frequently impossible to get sufficient exposure of the lower uterine segment in order to deliver the infant without considerable danger of opening the uterovesical fold of peritoneum. When the available space is obviously too limited to deliver the infant, without danger of peritoneal injury, we have recently deliberately incised the uterovesical fold, on the left side, as shown in Fig. 3. By this means free exposure of the lower uterine segment can be readily obtained regardless of how much the cervix is dilated or retracted. The free margins of

segment and is passed out through the lower angle of the uterine incision, where it is fixed in position, by one suture of No. 0 catgut. The lower end of this drain is allowed to protrude into the lower uterine segment and vagina for about four to five cm. At the end of five to seven days, it can be easily removed through the vagina. This step in technic allows dependent drainage of the space of Retzius. In the seven cases in which it has been used, there was a minimum of postoperative reaction and the abdominal wounds healed promptly.

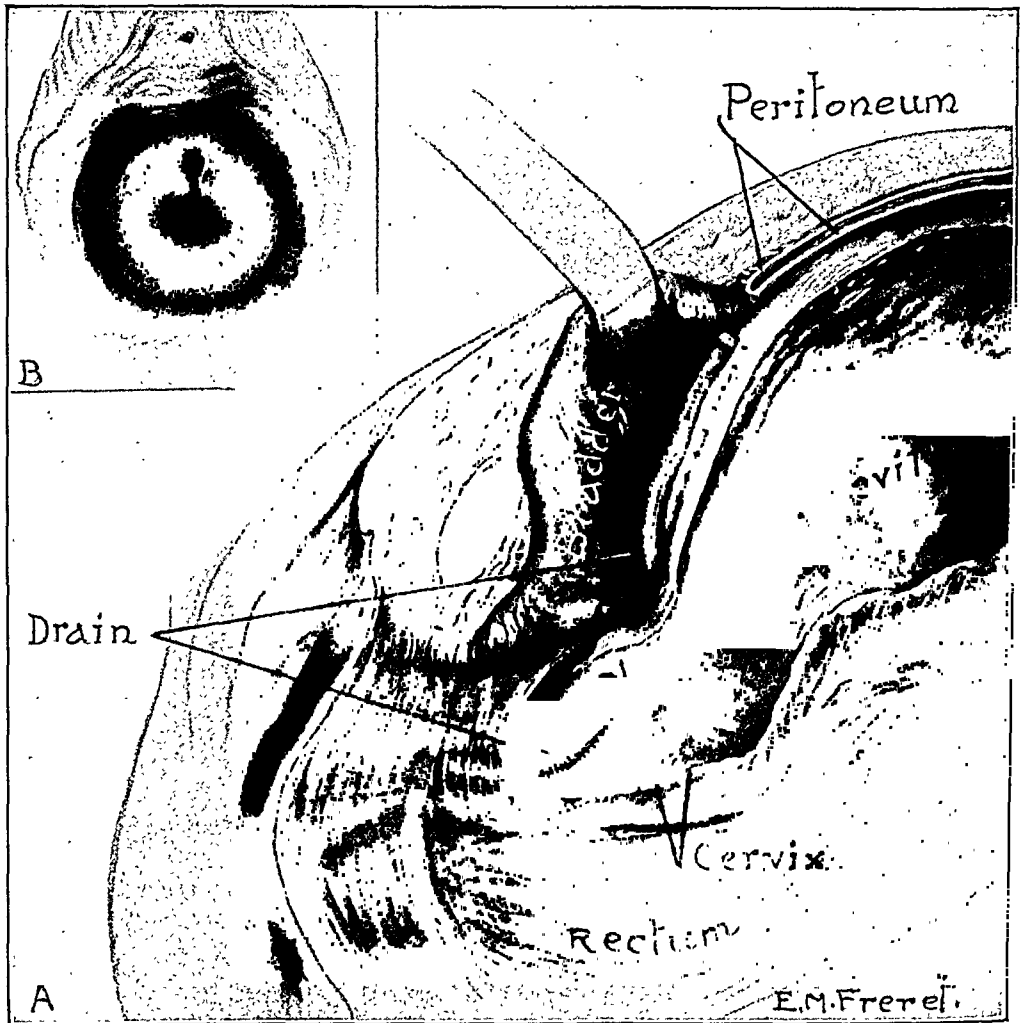


Fig. 5.—A, Diagram showing method of dependent drainage of space of Retzius, by drain passed through lower angle of uterine incision. Inset B shows observed drainage opening in anterior lip of cervix two weeks after operation.

Criticism of drainage through the lower uterine segment, possibly leaving a weak spot which might rupture during a future labor, is anticipated. In defense of this criticism, attention is called to the fact that the lower end of the uterine incision, used for the Latzko operation, always comes very close to the upper margin of the vagina. Inspection of the cervix following removal of this drain has shown it passing through the vaginal portion of the cervix as in inset "B," Fig. 5. Even

One of the most important steps in the technic of extraperitoneal cesarean section, to insure safety of the procedure and to promote satisfactory wound healing, is the establishment of adequate drainage of the space of Retzius. In the past it has been customary to use, for this purpose, one cigaret drain, which was placed beside the bladder, and passed

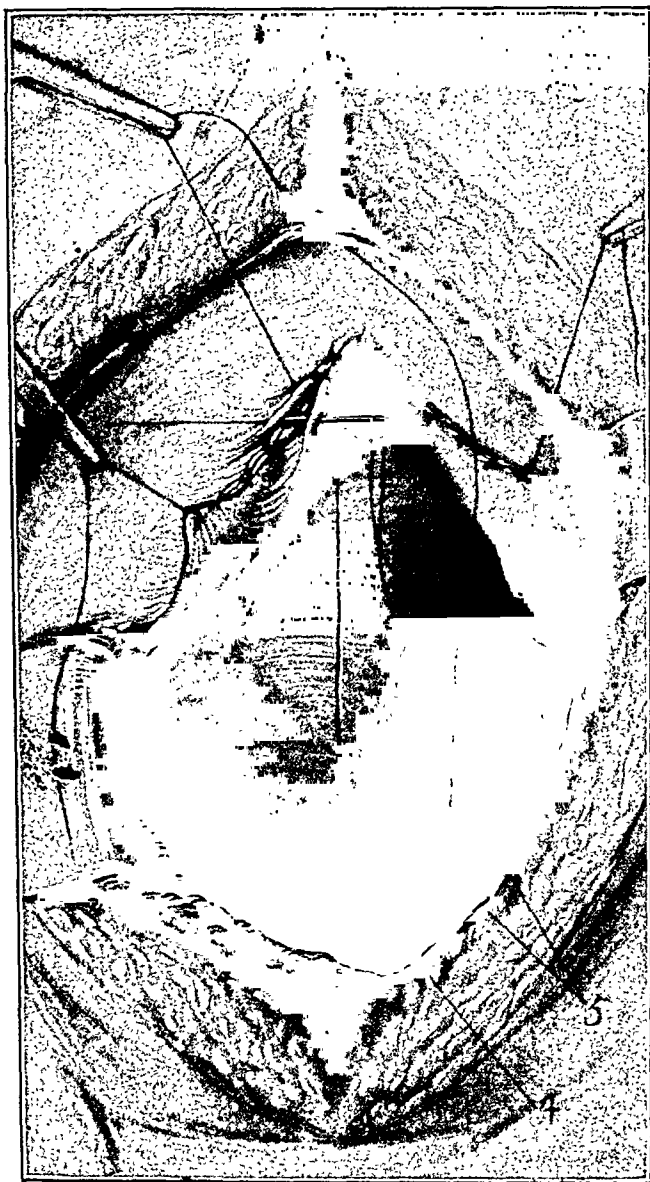


Fig. 4.—Method of closing incised uterovesical fold of peritoneum. 5, Incised edge of posterior layer of endopelvic fascial capsule of bladder.

out through the lower angle of the abdominal incision. This drain was removed after two to seven days and, in most cases, seemed adequate for the purpose. However, certain patients had profuse drainage and persistent troublesome drainage sinuses for some time after operation.

Recently, we have used, in addition to drainage through the lower angle of the abdominal incision, a second small cigaret drain as shown in Fig. 5. This drain is placed between the bladder and lower uterine

Table III is a summary of operative indications. Two-thirds of the patients operated upon had contracted pelves. In only one patient was the cervix fully dilated. In 26 of the 27 patients, the average cervical dilatation, at time of operation, was 4.8 cm. in spite of an average first-stage labor, in these cases, of 40.7 hours and an average duration of ruptured membranes of 38.8 hours. These patients had an average of four vaginal examinations before operation. Maternal exhaustion and evidence of fetal distress, in some cases, were factors influencing the decision to terminate labor. Two cases were successfully delivered of living children after attempted high forceps operations.

TABLE III. OPERATIVE INDICATIONS

Normal pelves, good labor, cervical dystocia	3
Normal pelves, inertia uteri, cervical dystocia	6
*Contracted pelves, good labor, cervical dystocia	6
Contracted pelvis, inertia uteri (fully dilated)	1
Contracted pelves, inertia uteri, cervical dystocia	11
	<hr/> 27
<i>Other Conditions at Time of Operation</i>	
Maternal exhaustion	4
Fever and tachycardia	6
Respiratory infection—toxemia	1
Fetal distress	8
Unsuccessful high forceps	2

*One operation done to protect premature (31 wk.) baby.

Table IV is a summary of data regarding anesthesia, duration of operations, wound drainage, and postoperative reactions. We can confirm the observations of other writers regarding the fact that, in spite of extensive dissection, a minimum of disturbance of bladder function accompanies the procedure.

The average weight of the babies delivered was 7 pounds, 9 ounces.

TABLE IV. SUMMARY OF THE 27 LATZKO OPERATIONS

Anesthesia: Gas-oxygen and ether, 26; gas-oxygen and spinal, 1	
Average duration of operations, 61 minutes.	
Drainage of space of Retzius:	
Abdominal	20
Abdominal and through uterine incision	7
Postoperative fever:	
Average duration	8.2 days
Average high point	102.3 degrees
Postoperative catheterization:	
None	8
Once to twice	13
Retention catheter for 48 to 72 hours	6
Weight of babies (3 pounds, 9 ounces to 10 pounds, 7 ounces):	
Average, 7 pounds, 9 ounces.	
Postoperative days in hospital:	
Average 18.1	

Table V shows the incidence of operative complications. In one case the bladder musculature was injured, while extracting the child, but the bladder itself was not opened. In another case, the finger of an assistant was accidentally pushed through the bladder wall while retracting the bladder manually. This accident

if the drainage opening persisted, which seems unlikely, it would weaken the wall no more than a deep cervical laceration. On the other hand nothing should insure good healing of the uterine incision, as a whole, so much as free postoperative drainage of the infected space between the bladder and lower uterine segment.

In the following six tables is recorded a summary of the data regarding 27 extraperitoneal (Latzko) operations done by eight members of the Woman's Hospital staff.

In Table I it will be noted that 22 of the 27 patients operated upon were at term with their first pregnancies; that two-thirds had contracted pelvis; that four had had previous complicated deliveries; and that five were toxic. Contracted pelvis, in this group of cases, were invariably borderline in type, justifying adequate trial labor.

TABLE I. SUMMARY OF DATA REGARDING LATZKO OPERATIONS PERFORMED FROM 1930 TO DATE

No. of patients	27
No. of operations	27
Elective operations	0
After trial labor	27
No. of operating surgeons	8
Average age of patients	29.4 years
History of pregnancies:	
Gravid i, 22; Para i, 2; Para ii, 2; Para iii, 1	
<i>Antepartum conditions</i>	
Type of pelvis:	
Normal	9
Justominor	9
Male or funnel	7
Simple flat	2
Toxemia	5
Previous complicated labors	4
Pyelitis	1
Congenital dislocation of hip	1

Table II is a summary of the progress of labor in the 27 patients at the time they were operated upon. It will be noted that the average duration of ruptured membranes was 40.7 hours; that the average duration of labor was 38.8 hours; and that in 21 of the 27 cases the head had failed to engage. More than two-thirds of the cases had some degree of uterine inertia. The average cervical dilatation was 4.3 cm. Considering these facts, there is little doubt that these cases should be looked upon as, at least potentially, infected at the time of operation.

TABLE II. SUMMARY OF FINDINGS, AFTER THE 27 TRIAL LABORS, AT TIME OF OPERATION

Onset: Spontaneous	24
Induced—Voorhees' bags—toxemia	2
Induced—rupture of membranes postmaturity	1
Type of labor: Good 8, fair 12, poor 7.	
Membranes: Intact 2, ruptured 25. Average	
duration of ruptured membranes (25 cases)	40.7 hr.
Average duration of labor	38.8 hr.
Presentation: breech 1, vertex 26.	
Level of presenting part: Engaged 6, unengaged 21.	
Average dilatation of cervix	4.3 cm.

uterine contractions. At time of operation she had a foul vaginal discharge. Soon after labor finally started, at thirty-one weeks, the baby showed signs of distress, and suprapubic delivery was resorted to as a means of saving the baby. Autopsy showed that death was due to bilateral bronchopneumonia, probably the result of aspiration before delivery.

TABLE VII. FOLLOW-UP

All wounds healed at 6 weeks after operation
Subsequent pregnancies, 3
1 Delivered by low flap cesarean section
1 Delivered by prophylactic low forceps
1 At present in antepartum clinic
<i>Mortality</i>
Maternal: 1 death
Condition satisfactory until tenth postoperative day. Died suddenly of coronary occlusion.
Fetal: 1 neonatal death
Premature (31 wk.) baby died 48 hours after birth. Autopsy showed bronchopneumonia, bilateral

In a recent article entitled, "The Abuse of Caesarean Section,"²⁴ a plea has been made for obstetricians to reduce the number of deliveries by this method and, when indications arise, to resort to the older obstetric procedures, such as craniotomy, internal podalic version, forceps, cervical incisions, and dilatation of the cervix by use of hydrostatic bags.

The disadvantages and dangers of these methods are too familiar to members of this society to need any discussion.

From our limited experience with extraperitoneal cesarean section, we are doubtful as to whether craniotomy, especially in a living child, is ever necessary.

On account of the dangers and unsatisfactory results of attempting to complete cervical dilatation by the use of hydrostatic bags, we have practically abandoned this method of treatment.

The advisability of manually completing cervical dilatation or resorting to cervical incisions, in order to terminate labor, must be decided in the individual case. We are convinced that these procedures are definitely unsuitable for some of the patients in whom the cervix has failed to dilate after prolonged first-stage labor.

Internal podalic version, which is attended by a high rate of fetal mortality and a high incidence of maternal and fetal birth injuries, has been used as a method of delivery for nearly every known obstetric complication. Fortunately, for both mothers and their babies, the indications for this procedure have diminished as refinements in operative obstetric technic have developed.

Undoubtedly some of the cases in this series, if handled in other obstetric clinics, would have been delivered by low flap cesarean section. In none of the patients, when studied individually, could it be denied that there would have been a real danger of infection if delivered through the abdomen.

was probably favored by overdistention of the bladder with fluid to assist in making the dissection. The uterovesical fold of peritoneum was accidentally opened in five patients.

TABLE V. COMPLICATIONS OF OPERATIONS

Bladder injuries:	
Musculature only	1 case
Bladder opened	1 case
Peritoneal injuries:	
Uterovesical fold opened	5 cases
Uterovesical fold opened deliberately to get exposure	3 cases

Table VI is a summary of postoperative complications. The most frequent complication was faulty wound union. One patient died of coronary occlusion, the only serious postoperative complication which occurred. Considering the type and physical condition of patients operated upon, we feel that, on the whole, they had surprisingly uneventful recoveries.

There was one neonatal death of a premature baby from bronchopneumonia.

TABLE VI. POSTOPERATIVE COMPLICATIONS

Maternal:	
Faulty wound union—1 wound resutured	8
Shock, mild	5
Nausea and vomiting	4
Upper respiratory infection	3
Pyelitis	2
Sapremia	2
Coronary occlusion (death)	1
Pleurisy	1
Toxic psychosis	1
Dermatitis (iodoform)	1
Retained secundines	1
Fetal:	
Prematurity (31 wk.) bronchopneumonia death	1

Table VII is a brief summary of the follow-up of patients operated upon and of the one maternal and one neonatal death which occurred in the series. Three patients had subsequent pregnancies.

The one maternal death occurred suddenly, of coronary occlusion, ten days after operation. Until this accident manifested itself, the patient was apparently making a satisfactory recovery. Her temperature was normal on the day that symptoms of coronary occlusion appeared. At time of operation, the cervix was 5 cm. dilated, and the head of the baby, weighing 7 pounds, 12 ounces, was just engaged in a R. O. P. position. The pelvis was normal in size. The membranes ruptured at the onset of fifty-four hours of first-stage labor. During the last eighteen hours, the contractions were frequent and hard. At time of delivery, she showed signs of exhaustion. She had fever, a rapid pulse, and had had chills.

The one neonatal death occurred forty-eight hours after delivery, in a baby delivered at thirty-one weeks of pregnancy, weighing 3 pounds, 9 ounces. The mother had had a previous premature labor at twenty-four weeks' gestation and was extremely anxious for this child. She had had uterine bleeding on several occasions during her pregnancy and had spent much of the time in bed. For two weeks before delivery she had had scant bleeding off and on and painful

DR. HENRY T. BURNS.—The advantages of this operation are becoming recognized and its popularity has increased rapidly during the past few years.

Fleischman and Kushner of the Bronx Hospital have recently reported a series of 19 cases with no maternal mortality.

Barnes of the Grace Hospital in New Haven has reported a series of 22 cases with no maternal deaths, and I believe he does the Latzko operation even as an elective procedure in some cases that have not been in labor.

In performing the Latzko extraperitoneal cesarean section 54 times, I have accidentally opened the peritoneum 7 times, but only once in the last 17 cases. I have never deliberately cut the peritoneum, but I can see where the method described by Aldridge may be of great help in very difficult cases. In getting the proper line of cleavage between the bladder and uterus, I have cut the endopelvic fascia transversely just below the peritoneal reflection, instead of longitudinally.

DR. JAMES F. NORTON (Jersey City, N. J.).—We have done 58 Latzko operations at the Margaret Hague Maternity Hospital in Jersey City. We have had one maternal death due to an injury to the patient's left ureter and subsequent death from sepsis. In the Margaret Hague Maternity Hospital, where we have a very large general service covering the entire County of Hudson, many patients are brought in that are impossible to handle in any manner except by some type of extraperitoneal operation.

I think that now practically all our operators isolate the posterior sheath of the endopelvic fascia in the same fashion as Aldridge has indicated. It was interesting to hear of Aldridge's method of handling the uterovesical fold of peritoneum. Cosgrove has utilized that procedure recently and he has gone so far in private conversation as to offer it as a modification of the technic of the Latzko section. I had not heard of it elsewhere until Aldridge described it tonight, but it has been utilized on the services in the Margaret Hague Maternity Hospital with no undue or untoward disturbances. We have not, as far as I know, used the vaginal type of drainage, all the patients being drained through the lower angle of the wound.

Ghosh, Datta and Adya: A Preliminary Observation on the Pharmacology of Ergometrine, *J. Indiana M. A.* 5: 519, 1936.

Dudley and Moir in 1935 isolated an alkaloidal substance which differs from ergotoxine chemically and pharmacologically and which they named ergometrine. Almost simultaneously scientific journals in Britain, America, and on the Continent announced the isolation of a similar new alkaloid from ergot. They have been described under the names of ergometrine, ergotocin, ergostetrine, ergobasine, and ergometrinine.

The action of the new alkaloid differs from the alkaloid of the ergotoxine group in that the effects are produced in five to eight minutes when given by mouth, three to four and one-half minutes when given intramuscularly, and within a minute when given intravenously. The toxicity is low and no untoward symptoms follow its use over a prolonged period.

The authors conclude that: (1) Ergometrine has very little effect on the non-gravid uterus. (2) It causes powerful contractions of the gravid uterus but does not throw the uterus into tetany. (3) It stimulates the heart directly, making the beats stronger and quicker. (4) It causes a slight rise of blood pressure which, though not very high, is marked. (5) It has no gangrene effect like ergotoxine due to lack of peripheral vasoconstriction.

F. L. ADAIR AND S. A. PEARL.

Success with the extraperitoneal (Latzko) cesarean section demands:

1. Obstetric skill and experience to select cases with proper indications for the procedure.
2. A thorough knowledge of the anatomic relationships about the bladder and lower uterine segment.
3. Training and experience in surgery as well as obstetrics, in order to apply successfully the procedure, and to avoid unnecessary surgical complications.

From our limited experience with the Latzko operation we are convinced that when proper indications arise:

1. It is an invaluable procedure for the suprapubic delivery of infected or potentially infected cases.
2. The method of approach, for extraperitoneal cesarean section, offered by the Latzko technic, is anatomically the most logical one yet developed.
3. The technic of the procedure is safe and not too difficult for those well trained in gynecology as well as obstetrics.
4. Bladder injuries can be prevented by a knowledge of the endopelvic fascia and dissection in the proper planes of cleavage.
5. In order to get adequate exposure of the lower uterine segment, and to prevent accidental injury to the peritoneum and contamination of the peritoneal cavity, it may be wise in certain cases, to incise the utero-vesical fold of peritoneum deliberately, by the method described, before the uterine cavity is opened.
6. Dependent drainage of the space of Retzius will promote healing of the uterine and abdominal incisions and increase the safety of the procedure.
7. Maternal mortality, from cesarean section, could be reduced, if obstetricians would familiarize themselves with the technic of the extraperitoneal operation, and refuse to adopt the abdominal route in cases where preoperative conditions, known to favor uterine infection, have existed.

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DISCUSSION

DR. KYLE B. STEELE.—Some time ago, in performing a Latzko section, I found that the space which could be exposed in the lower uterine segment was entirely inadequate. On the spur of the moment, I resorted to a Y-shaped incision, the limbs of the Y being placed below the peritoneal reflection. I found that this move provided adequate room. I have tried this modification since that time, and feel that it is a very valuable procedure where there is a lack of space.

origin and not due to gluttony or lack of exercise. For, in the first place, there was nothing to suggest that the food intake or exercise of the patients with toxemia differed from that of the controls; indeed, many of our patients were obese in spite of strenuous dieting. Second, there was a very high incidence of other endocrine stigmas in the obese individuals.

2. DISTRIBUTION OF HAIR

In the female, abnormalities in the distribution of hair resulting from endocrine disturbances are of two types: (1) An increase in the amount of hair, with a tendency to male distribution, that is on the legs, thighs, abdomen, chest, face, and occasionally around the nipples; (2) Decrease in pubic and axillary hair so that it is scanty, very fine and silky, and sometimes almost absent. These two types of abnormality in hair distribution due to endocrine disturbances were present, with almost equal frequency, in 74 per cent of the patients with toxemia, as compared to only 9 per cent of the normal controls.

3. STATURE

Various observers have noticed that a high proportion of women with toxemia of pregnancy are of stocky build. The coincidence of short, thick-set framework and obesity gives many of these women a characteristic appearance. There are some patients, however, that have an unusually large bony framework (Fig. 1). Definite abnormalities of stature were present in 65.8 per cent of the toxemia patients as contrasted with 21.0 per cent of the normal patients. It was found that the average weight/height ratio of patients in the normal series was 2.08 pounds per inch and that of patients in the toxemia series 2.5 pounds per inch (Fig. 4). Such peculiarities of stature are generally regarded as due to aberrations in the function of the endocrine glands.

4. FACIES

An outstanding characteristic of most of our patients with toxemia of pregnancy was that they looked several years older than their chronologic age (Fig. 2). Some young women of twenty to twenty-five years appeared thirty to forty years of age. This appeared to be due to the combination of obesity, statural peculiarity, and change in facies. They had enlarged features of the acromegaloid type, which in many were of long standing, and in others had appeared during the antepartum course. The most common change in the features was enlargement of the nose. These facial changes were sometimes associated with enlargement of the hands and feet. Their development was almost always noted by the patient or her companions, and often progressed noticeably under clinical observation. It is true that in normal pregnancy there is some enlargement of the features, generally attributed to physiologic hyper-

THE ENDOCRINE BASIS OF TOXEMIA OF PREGNANCY*

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IN THIS paper we desire to present evidence to support our belief that the so-called toxemia of pregnancy is a manifestation of a disturbance of the endocrine glands.

The observations here recorded have been carried out over a period of four years. They have led to the conclusion that in the large majority of instances toxemia of pregnancy occurs in women with a constitutional habitus, in itself a manifestation of an endocrine disturbance.

Our primary criterion for the diagnosis of toxemia of pregnancy was the development in the later months of pregnancy of abnormally high blood pressure, in women in whom there was no history or other evidence of preceding renal or hypertensive disease. It may well be that there are cases of toxemia of pregnancy in which hypertension is absent and the disorder is manifested solely by edema and albuminuria. But in order to deal with a criterion of the disease which is practically universally accepted, we have included only patients with high blood pressure. All our patients began pregnancy with normal blood pressure and developed a systolic pressure exceeding 140 mm. and a diastolic pressure above 90 mm. Almost every patient had a blood pressure well over this level. The present study is based on 120 patients fulfilling this criterion. As controls, we have used 100 consecutive patients having normal pregnancies. The evidence is presented under the following headings: (1) Body weight, (2) hair distribution, (3) stature, (4) facies, (5) form of pelvis, (6) basal metabolism, and (7) blood proteins.

1. BODY WEIGHT

The pregestational weight of women with toxemia of pregnancy averages much more than that of a similar number of normal pregnant women (Fig. 3). The average weight in the normal series was 126.2 pounds, as contrasted to the average weight in the toxemia series of 148 pounds. The high incidence of obesity in patients who develop this disease is thus demonstrated. Moreover, in a large proportion of these cases there was a tendency to obesity from an early age. It is a well-known fact that patients with toxemia of pregnancy gain weight excessively. Further evidence indicates that this obesity is of endocrine

*Read at a meeting of the New York Obstetrical Society, October 13, 1936.

and primitive type of pelvis in the toxemia series is very high. The rôle of the hormones in the evolution of pelvic types has been ably postulated by Caldwell, Moloy, and D'Esopo.¹ Since we find that women of extreme endocrine types in the great majority of cases have pelvises that fall into the android and anthropoid class, we may speculate that this reversion to the male and primitive type of pelvis is due to an inherent imbalance in the hormonal system.

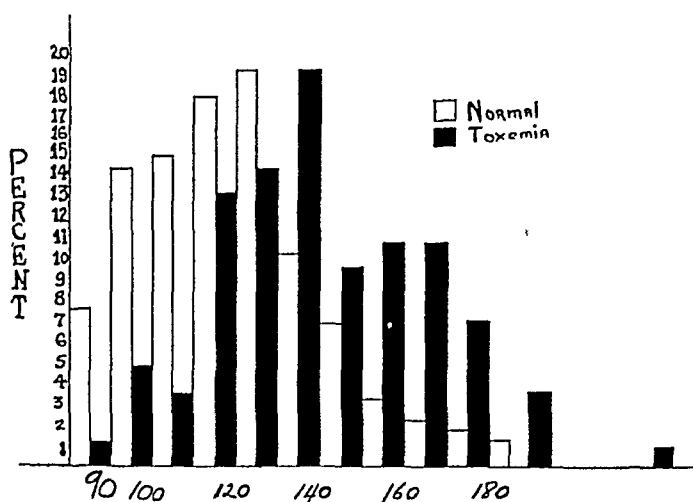


Fig. 3.—Pregestational weight of patients with toxemia and normal controls. Note the preponderance of toxemia among the obese.

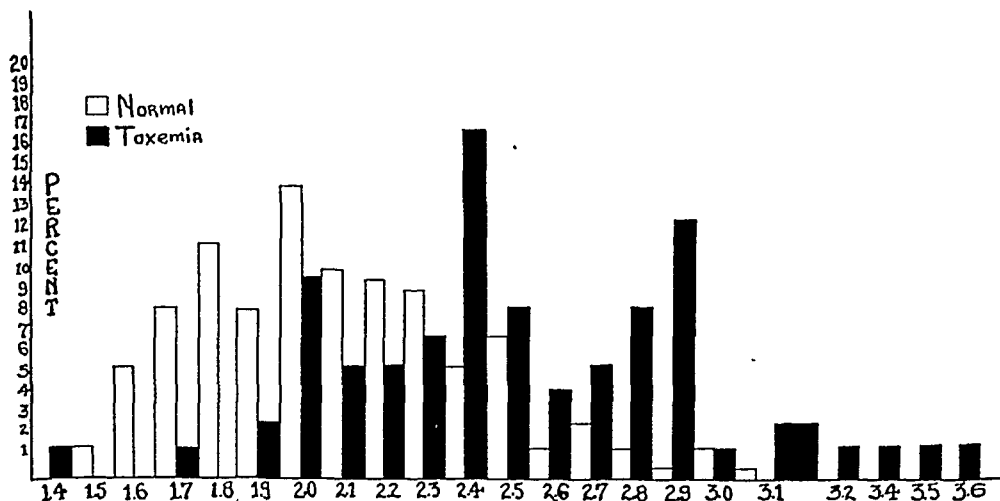


Fig. 4.—Pregestational weight/height ratio of patients with toxemia and normal controls, demonstrating the high incidence of obesity among the former.

We must further comment on the unusual number of large pelvises which appear to be more common than in our normal series. Some border on giantism, with dimensions far out of proportion to the stature of the patient (Fig. 5).

We wish to report a final observation relative to the separation of the symphysis during the antepartum period. Although the average separation, as seen stereoscopically, is not greater in the toxemia group than in the normal, in 7 cases this physiologic relaxation of the joint was by far

activity of the pituitary gland. This is rarely marked enough to become a complaint, as it was in some of our cases of toxemia of pregnancy. It was found that 55 per cent of the latter had changes in facies, whereas such changes occurred in only 5 per cent of the normal patients.

5. FORM OF PELVIS*

In the course of evaluating pelvic x-rays one year ago, we were aroused by the infrequency of the true gynecoid pelvis in those women who developed toxemia of pregnancy. Of 23 pelvises in toxemic women, only 2

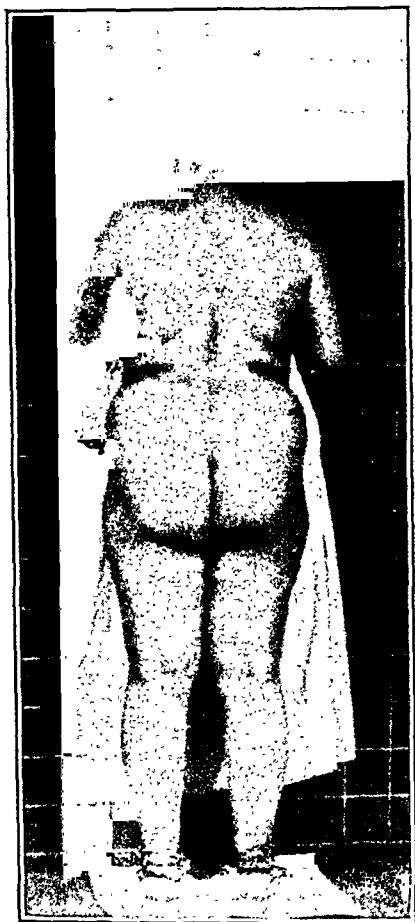


Fig. 1.



Fig. 2.

Fig. 1.—Showing stocky build and girdle obesity in a woman of twenty-six years, with toxemia of pregnancy. (Photograph taken two weeks postpartum after loss of 20 pounds.)

Fig. 2.—Facies of patient in Fig. 1.

were gynecoid. Since this observation, we have x-rayed routinely all patients who developed toxemia to determine the correlation, if any, between their body habitus and pelvic architecture (Table I).

The most striking feature of this survey is the low incidence of the gynecoid pelvis and the predominance of other types, especially the anthropoid. The table shows that the incidence of reversion to the male

*We desire to express our sincere thanks to Drs. I. Seth Hirsch and Myron A. Schwartzchild for their aid with the roentgenologic aspects of this study.

6. BASAL METABOLISM

A number of investigators³⁻⁷ have shown that in uncomplicated pregnancy the basal metabolic rate is increased 10 to 30 per cent above normal. This is especially true in the later months of pregnancy. It

TABLE I. SHOWING PELVIC TYPES IN THIS SERIES

TYPE	NUMBER OF CASES	PER CENT FOUND IN TOXEMIA	PER CENT FOUND BY CALDWELL, MOLOY AND D'ESPO
Anthropoid	25	30.1	11.6
Gynecoid with anthropoid	13	15.7	4.6
Anthropoid with gynecoid	3	2.6	6.5
Android	14	16.6	11.6
Android with gynecoid	5	6.0	5.1
Android with anthropoid	8	9.6	3.7
Platypelloid	3		
Platypelloid with gynecoid	2	6.0	0.9
Gynecoid	6	7.2	39.5
Gynecoid with narrow forepelvis	4	4.8	11.1

should further be borne in mind, in this connection, that all our patients had high blood pressure, and it is well known to internists that in so-called essential hypertension there is a tendency to elevation of the metabolic rate. Hence, in hypertensive toxemia of pregnancy one would anticipate, a priori, a high basal metabolic rate by virtue of two factors, pregnancy and hypertension. It is, therefore, of interest and undoubtedly significant that in 35 patients with toxemia of pregnancy, in whom repeated observations of the basal metabolic rate were made, we found that 68 per cent had basal metabolic rates below plus 10 per cent, which is the accepted lower limit of normal during pregnancy (Table II).

TABLE II. SHOWING BASAL METABOLIC RATES IN CASES WITH TOXEMIA

CASE	PRIMIPARA	CASE	MULTIPARA	PER CENT BELOW +10%
1	+19	18	+13	Primipara
2	+30	19	+15	65%
3	- 3	20	-15	Multipara
4	+ 4	21	- 4	72%
5	+ 3	22	- 5	Total
6	+13	23	+15	68%
7	- 4	24	- 9	
8	- 8	25	+ 2	
9	+12	26	+15	
10	-10	27	+18	
11	+16	28	- 9	
12	-11	29	- 8	
13	+19	30	- 4	
14	- 3	31	+ 5	
15	+ 2	32	- 1	
16	- 2	33	- 2	
17	+ 3	34	- 3	
		35	+ 2	

wider than any of a series of 150 normals (Fig. 6). In view of the accepted work of Abramson and coworkers,² this may indicate an abnormal endocrine function in these patients, although further observation on a larger series is necessary for verification.

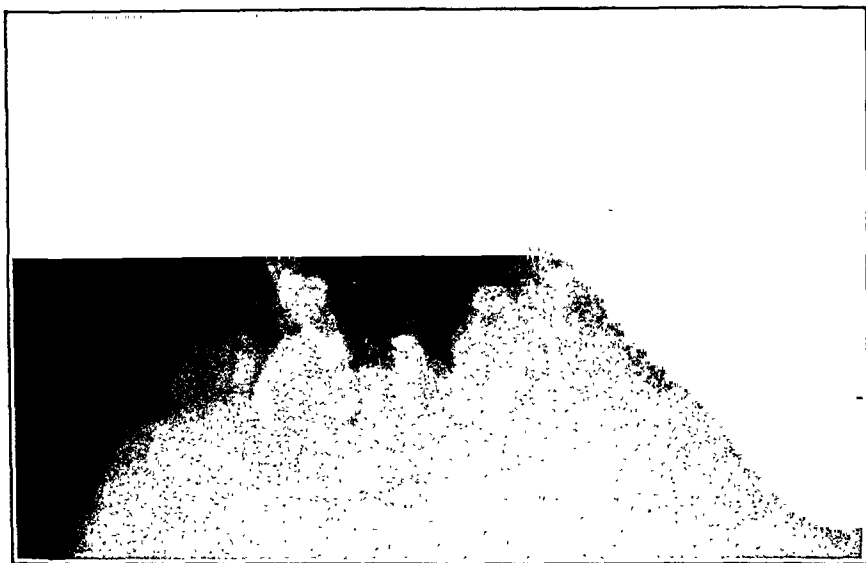


Fig. 5.—X-ray of pubic arch of a large platypelloid pelvis. Note tremendous sweep of pubic arch and rami. Bis-ischial diameter 16.0 cm. Wide separation of symphysis (not demonstrable in this view) also present. Case of recurrent toxemia with marked endocrine stigmas.

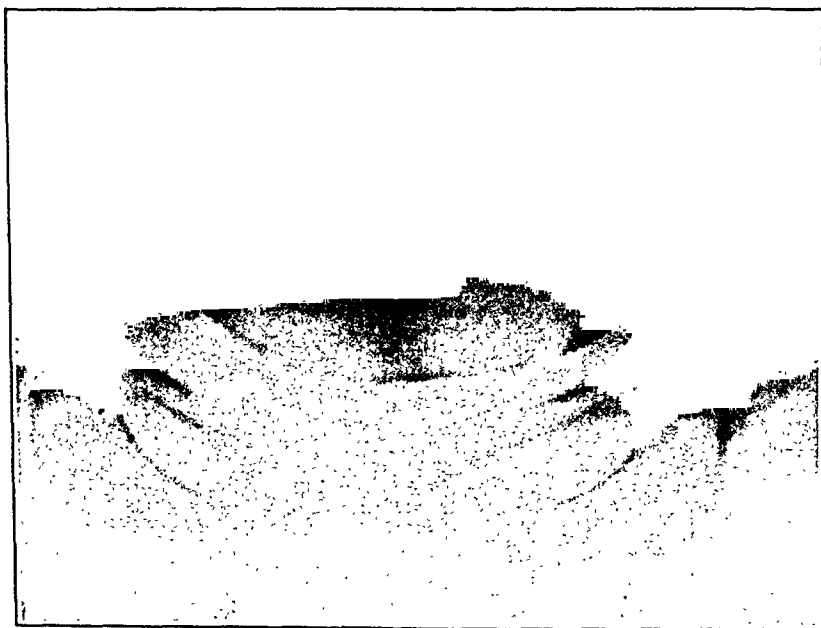


Fig. 6.—X-ray of symphysis in case of patient with toxemia, showing marked antepartum separation of symphysis. Patient of extreme endocrine type.

The observations on the form of pelvis thus add very strong evidence to the impression that toxemia of pregnancy occurs in a woman of definite constitutional habitus, due probably to dysfunction of the endocrine system.

Since the depression in the protein content of the blood in some cases occurred without significant albuminuria or dietary deficiency, it seems probable that it was a manifestation of an endocrine disturbance.

TOXEMIA OF PREGNANCY AND RENAL FUNCTION

Parenthetically, we would like to interpolate a few words regarding the relation of toxemia of pregnancy to impairment of renal function. *In not one of 120 patients with toxemia of pregnancy was there significant impairment of renal function.* Of course, patients who entered pregnancy with glomerulonephritis are not included in the category of toxemia of pregnancy. Renal function was studied by the concentration test and by the determination of the nonprotein nitrogen of the blood. All the patients were able to elaborate urine of specific gravity 1.020 or more, which rules out significant impairment of renal function (see Fishberg).¹¹ The nonprotein nitrogen of the blood was also within normal limits. In the light of these facts, theories regarding impairment of renal function as a factor in the pathogenesis of the toxemias of pregnancy are, as has been realized by most recent students, to be discarded. Moreover, impairment of renal function need not be taken into consideration in the treatment of the toxemia of pregnancy. In the natural history of this disease, impairment of renal function does not appear during the pregnancy. It may appear after many years as a secondary consequence of the hypertension, just as it may result from long years of essential hypertension.

DISCUSSION

Summarizing the data just presented, it is found that 98 per cent of our patients with toxemia of pregnancy revealed evidence of one or more of the endocrine stigmas under consideration, and in a large majority there were two or more. The significance of these endocrine stigmas in women with toxemia of pregnancy is all the more evident on comparison with the normal controls. Only 15 per cent of the latter presented any endocrine stigmas and only 3 per cent had more than one stigma. The fact that 15 per cent of our normal controls presented endocrine stigmas does not militate against their significance in the toxemic cases. Our conception is that these stigmas are merely evidences of an endocrine disturbance, often constitutional in nature, which predisposes to the development of what is known as toxemia of pregnancy. That the actual disorder does not become clinically manifest in every individual with the underlying endocrine disturbance is not surprising, in fact would be anticipated, and has many analogies in clinical medicine. Of several sons of parents with diabetes and obesity, only some may actually develop glycosuria even though all are obese and show diminished sugar tolerance. The individuals with the endocrine stigmas described are al-

Since the main control of the metabolic rate rests in the endocrine glands, such a relatively low metabolic rate is indicative of an endocrine disturbance.

In two instances, we had the opportunity of observing the development of toxemia of pregnancy, in patients following the fall in metabolic rate that took place, in the one instance "artificially" as a result of thyroidectomy, in the other spontaneously. The first patient was a primipara who had had a thyroidectomy for Graves' disease in the fourth month of pregnancy. Following this procedure, the basal metabolic rate, which had previously been high, fell to minus 20 per cent. This patient, who had had a normal blood pressure and urine, subsequently developed copious albuminuria and hypertension. The second case was also a primipara who had had a basal metabolic rate of plus 20 to 26 per cent on several occasions for two years prior to her pregnancy. Instead of increasing during the pregnancy, as it normally does, the basal metabolic rate fell to minus 3 per cent and she developed hypertension of 150/100 mm.

7. PLASMA PROTEINS

Chemical studies of the blood in the toxemias of pregnancy have revealed a fairly constant abnormality in the concentrations of the plasma proteins. It has been definitely shown by many authors^{8, 9} that the plasma proteins are diminished in these cases, and that this diminution is absolute and not due to dilution.¹⁰ We corroborate these findings. In 15 of the 17 patients in whom this determination was made (Table III) the plasma protein concentration was depressed to between 4.07 and

TABLE III. SHOWING PLASMA PROTEIN DETERMINATIONS IN 17 CASES OF TOXEMIA, OF WHICH 1 TO 7 ARE PRIMIPARAS, THE REMAINDER MULTIPARAS

CASE	TOT. PROT.	ALBUMIN	GLOBULIN	A/G RATIO
1	5.51	3.05	2.46	1.2
2	4.07	2.61	1.46	1.7
3	4.68	2.25	2.43	0.92
4	4.93	2.39	2.54	0.9
5	5.20	2.50	2.70	0.92
6	4.25	2.81	1.44	1.9
7	4.68	2.34	2.34	1.0
8	5.06	2.81	2.25	1.2
9	5.20	3.75	1.45	2.5
10	5.91	3.51	2.50	1.4
11	5.51	3.12	2.39	1.2
12	6.25	3.95	2.30	1.7
13	5.51	2.73	2.78	0.98
14	5.85	3.12	2.73	1.2
15	4.93	3.21	1.72	1.2
16	4.93	2.34	2.59	0.9
17	6.25	3.12	3.13	1.0

5.91 gm. per cent as contrasted with normal limits of 6 to 8 gm. per cent. There was also inversion of the albumin/globulin ratio in 6 cases and a tendency toward inversion in 6 others. It is well known that abnormalities of the endocrines sometimes affect the level of the blood protein.

seizure. In our hands the most efficient treatment of the toxemia of pregnancy has been a regimen which tends to dehydrate the organism. The patient is put on a salt poor diet and the fluid intake is restricted to 1,000 c.c. or less. What is especially to be emphasized is that protein intake is not limited; in fact, especially in patients with considerable albuminuria, we give as much as 100 gm. of protein daily. It should be remembered that the plasma proteins are generally low in the toxemia of pregnancy, and this favors the formation of edema; ample protein intake is essential to combat the lowering of the plasma proteins and thus tend to avert or remove edema. There need be no fear of nitrogen retention because of the high protein intake; renal function is not significantly impaired. Other dehydrating measures which we employ are the frequent administration of magnesium sulphate by mouth with resultant abundant watery stools and the use of thyroid extract in those cases having a low basal metabolic rate. The latter is indicated not only by the tendency to water retention, which it combats, but by the relatively low basal metabolism. The usual bed rest and mild sedation with chloral and bromides or phenobarbital are also employed. In patients with great hypertension in whom convulsions or other cerebral symptoms seemed to impend, or with actual eclamptic convulsions, we have found the intravenous administration of magnesium sulphate of great value in addition to the other usual routine procedures.

Using the "dehydrating regime" just described, we have obtained splendid results in the large majority of patients with so-called pre-eclampsia, with clearing up of edema and fall in blood pressure. In the past four years convulsions did not develop in any patient with pre-eclampsia treated by this regime in our service at the Jewish Maternity Hospital. However, we should like to emphasize the fact that we do not believe that patients should be "carried along" on a medical regime for a long time. Our findings corroborate the important studies of Harris,¹⁵ Peckham,¹⁶ Corwin and Herrick,¹⁷ and Herrick and Tillman,¹⁸ who have shown that a high proportion of patients with toxemia later develop hypertensive disease with resultant shortening of life. There is some reason to believe that the chances of developing hypertension in later life are augmented by allowing the toxemia to persist for too long a period. For the sake of the mother later in life, she should not be allowed to remain in a toxemic state any longer than necessary.

CONCLUSIONS

Evidence is presented which, we believe, indicates that toxemia of pregnancy is an endocrine disturbance evolving in women with a pre-existent constitutional abnormality of the endocrine glands. The evidence consists in the following:

ways to be considered as potential victims of toxemia, which may develop only in one of their later pregnancies. This statement is borne out by the well-known fact that multiparas may develop toxemia despite previous normal pregnancies. The evidence here presented adds support to the theory that toxemia of pregnancy is a condition developing on the basis of a disturbance of internal secretion.

We do not feel that the observations here recorded throw any light on the precise nature of the endocrine disturbance which produces the toxemia of pregnancy. All the endocrine glands are interrelated and the function of all of them is affected in pregnancy. The available evidence does not permit a decision as to which of the endocrine glands is primarily at fault in the production of the toxemia of pregnancy. The work of Anselmino and Hoffmann,¹² purporting to show that the blood of patients with toxemia of pregnancy contains an excess of a pressor and antidiuretic principle secreted by the pituitary gland, has failed of confirmation.¹³ On the other hand, the recent work of Smith and Smith,¹⁴ revealing the presence of an excess of prolactin in the toxemia of pregnancy, is carefully controlled and to be accepted; it may well prove the starting point of more intimate knowledge of the nature of the endocrine disturbance underlying the toxemia of pregnancy, but does not as yet show how this disturbance is initiated.

THERAPEUTIC AND PROPHYLACTIC IMPLICATIONS

Since the large majority of cases of toxemia of pregnancy develop in women who present detectable evidences of endocrine dysfunction, one has a basis in the antepartum clinic for the segregation of those women who are most likely to develop toxemia. Our observations indicate that about 30 per cent of women presenting the endocrine stigmas described above (stocky framework, obesity, abnormal distribution of hair, etc.) ✓ will develop toxemia of pregnancy. In the past six months we have observed 34 women with such endocrine stigmas but no evidences of toxemia develop definite toxemia of pregnancy. We feel that if women with endocrine stigmas are segregated in antepartum clinics and carefully watched, one will observe the inception of the vast majority of cases of toxemia of pregnancy. This will afford the opportunity not only to undertake appropriate measures of therapy at the time when they are most useful, but also to study the pathogenesis of this disease.

The following may be said regarding the therapeutic implications of the fact that the toxemia of pregnancy is a result of endocrine dysfunction. While the precise nature of the endocrine disturbance is unknown, it is manifested by water retention in the organism. This water retention not only produces palpable edema, but it also may go on to the edema of the brain which is concerned in the production of the eclamptic

DISCUSSION

DR. RAPHAEL KURZROK.—The whole subject of the interrelationship between the endocrine glands and toxemia of pregnancy was, I believe, first noted about twenty years ago, by Hofbauer. He, at that time, postulated the theory that the pituitary gland and the adrenals in association with a placental factor, the so-called biogenous amines, substances of high pharmacologic potency, were interrelated with the toxemia of pregnancy. Only the first part of his theory has been taken up and investigated.

Among the symptoms of toxemia, hypertension and edema are notable, as the result of a hyperproduction of one or possibly two of the hormones of the posterior pituitary gland. In the posterior pituitary gland we have a group of hormones, one of which, oxytocin, has to do with the contraction of the uterus, and has no bearing on the problem at hand. The other has a combination of activities, probably residing in two molecular groups: the first raises the blood pressure, the second inhibits diuresis. Another substance, possibly arising from the middle portion or the pars intermedia of the pituitary gland, has an effect on the melanophore groups of certain species. Anselmino and Hoffmann stated that the retention of water and the hypertension can very well be due to an overproduction of the hormone which produces exactly these two phenomena and whose origin is in the posterior pituitary gland. Unfortunately, they worked with the rabbit, which is notoriously unreliable, especially so far as this particular type of testing is concerned.

The next important advance in this field was made by Cushing, who noted, in six cases of eclampsia, that there was direct invasion on the part of basophilic cells from the anterior pituitary gland and pars intermedia into the posterior pituitary gland, and that in the invasion of the posterior pituitary gland these cells underwent a process of degeneration and formed the amyloid substances or Herring bodies. He postulated, in addition, that the substance, vasopressin, arises from the anterior pituitary gland, because histologically, the posterior hypophysis does not appear like a secreting tissue. This view is of importance, because the anterior pituitary is that portion which enlarges during pregnancy. Cushing's concept has, however, recently been attacked in the work of Geiling and Lewis, and others. They have demonstrated that pure tissue cultures from the anterior pituitary gland contain neither the substance that raises blood pressure nor the substance that inhibits diuresis, nor the melanophore-expanding hormone. On the contrary, pure tissue cultures, arising from the posterior pituitary gland, produced both vasopressin and the melanophore-expanding substance.

The other work which has been amazingly interesting in this field has been that of Smith and Smith of Boston, who demonstrated that in true toxemia of pregnancy there is a marked increase in the amount of prolan and a lowering in the amount of estrin of both the blood and the urine. At the present time we do not know whether the increase in prolan is a cause, or the result, of toxemia. It is very interesting to note that the lowering of the plasma of proteins is a usual concomitant of a lowered basal metabolic rate which has been found to accompany most of these cases of toxemia of pregnancy.

More recently the adrenal has been drawn into the picture of toxemia of pregnancy by Fauvet. The adrenal is one of the glands of internal secretion that markedly enlarges during pregnancy. In toxemia of pregnancy and especially in eclampsia, however, there is a distinct diminution in the size of the cortex of the adrenal, and possibly some cases of death from toxemia of pregnancy unassociated with convulsions, may be due to a failure on the part of the adrenal.

The general concept that offers the most potent possibilities is perhaps one comparable to, but opposite in effect to, our view of the menopause. The menopause is due to a derangement of the glands of internal secretion because of the permanent

1. The average prepregnancy weight of patients that developed toxemia is 21.8 pounds more than that of patients in the normal series. The incidence of obesity in this type is great.

2. A high percentage of women with toxemia have abnormal distribution of hair.

3. Sixty-five and eight-tenths per cent of patients with toxemia have abnormalities of stature as contrasted with 21 per cent of controls. The average weight/height ratio of the normal series was 2.08 as compared to that of 2.5 for the toxemia series.

4. Fifty-five per cent of women with toxemia had changes in facies of the "acromegaloid" type as contrasted with 5 per cent of the controls.

5. Eighty-eight per cent of our cases with toxemia showed reversion to the male and primitive type of pelvis. Giant pelvis were unusually frequent.

6. Basal metabolic rate in toxemia of pregnancy averages definitely less than in normal pregnancy.

7. As has previously been demonstrated by others, the plasma proteins in toxemia of pregnancy are depressed below those in normal pregnancy.

8. In 98 per cent of our patients with toxemia of pregnancy there were one or more endocrine stigmas, and in a large majority there were two or more. Only 15 per cent of the normal controls presented any endocrine stigmas and only 3 per cent had more than one stigma.

9. In not one of our series of 120 cases of toxemia of pregnancy was there significant impairment of renal function as demonstrated by the concentration test and by the determination of the nonprotein nitrogen of the blood.

10. All pregnant women having endocrine stigmas should be considered as potential victims of toxemia. It is advised that they be segregated for investigation and proper therapy. The latter consists mainly in a regime of dehydration.

11. In "carrying along" a patient with toxemia of pregnancy, the fact should be seriously considered that a high proportion of patients later develop hypertensive disease with resultant shortening of life.

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PATHOLOGY

The right ovary was the site of the newgrowth in 33 instances, the left in 34. Both sides were involved in 12 or 15.2 per cent of our patients. As a result 91 specimens were available for study. Since the opposite ovary had been removed previously for a dermoid in two women, bilateral involvement really occurred in 14, or 17.7 per cent, of our cases. The smallest tumor was 4 mm. in diameter and the largest measured 40 by 25 cm., their average size being 9.5 cm. The contents of the cyst cavities were as follows: sebaceous material and hair in 81, sebaceous material alone in 6, and only hair in 2. One cavity was filled with hair mixed with a gelatinoid material. Seventy-three tumors showed the characteristic anlagen. These included calcareous substances, such as teeth in 18, bone in 13, and teeth in combination with bone in 8. Therefore, 39, or 49.4 per cent, revealed calcareous deposits. It was interesting to note that in none of the bilaterally involved cases was calcium seen in both ovaries. On microscopic examination, the well-differentiated adult structures which have been described frequently were demonstrated (Fig. 1). We encountered thyroid tissue in 9 cases and in one instance it was present on both sides (Fig. 2). The frequent association of pseudomucinous cysts with dermoids, noted by Blair-Bell¹ and Shaw,² was not observed in our material. We had but one case. The most common associated pelvic pathology was multiple fibroids of the uterus which occurred in 17.7 per cent. This figure corresponds with the expected frequency of fibroids in any gynecologic series.

SYMPTOMATOLOGY

In reviewing the literature, one is impressed by the varying opinions concerning the symptoms produced by these neoplasms. Lynch³ attributes little significance to the symptoms of dermoids. He states "symptoms might be slight or absent, though occasionally the patient may sense a weight in the pelvis, or complain of bladder and rectal discomfort." In Table I, the symptoms noted in Marshall's⁴ 415 cases are compared with those in our series.

TABLE I

	CASES	LOWER ABD. PAIN	BACK- ACHE	PRESSURE ON BLADDER OR RECTUM	TUMOR MASS	MENSTRU- AL ALTERA- TION
Marshall	415	48.0%	18.0%	27.0%	23.5%	12.0%
L. I. C. H.	79	65.5%	17.6%	30.6%	12.6%	7.5%

The frequency of pain and pressure, we feel, is due to the effect of the size, the location, and the relation of the tumor to other structures. The vast majority of dermoids grow slowly, and as a rule, reach moderate size. Their average diameter, in our material, was 9.5 cm. Due to their weight they usually remain in the pelvis, but because of their long pedicle, marked mobility is possible and as a result they frequently lodge in either the anterior or the posterior culdesac. This localization of the tumor in the pelvis often is aided by their becoming densely adherent to either the rectum or the bladder. Hence by virtue of their position, lower abdominal pain with pelvic pressure is to be expected. The long pedicle also permits displacement upward into the abdominal cavity with sufficient force to permit its recognition by the patient and spontaneous dislocation is often produced by sudden changes in posture. This was noted in 10, or 12.6 per cent, of the cases.

Menstrual disturbances were rare. In five, amenorrhea was due to an associated pregnancy. Five other patients complained of irregular bleeding while one experienced polymenorrhea. This lack of menstrual abnormalities may be explained by

loss of one of these glands (the ovary). On the other hand, in pregnancy, a new gland of internal secretion in form of the placenta has been added. A re-arrangement must take place, the nature of which depends a great deal upon the individual's constitutional make-up, and endocrine equilibrium. Hence, the derangement thus induced in the pregnant woman will vary from patient to patient. In one it may be an overstimulation of the posterior pituitary gland, in another a failure of the adrenal cortex (hyperemesis?), in a third hyperthyroidism, in a fourth a tachycardia due to disturbance of the autonomic nervous system, etc.

DR. ROBERT T. FRANK.—No one can take exception to the extremely interesting clinical type presented this evening. The numerical preponderance of this group may be of significance, although the stigmas presented are very common. That they should appear in such numbers in this group proves at least that these individuals are more easily affected by disturbances, the nature of which I am unwilling to attempt to analyze, than other groups. If these gentlemen will take the time and the trouble, because much is involved, to study this group further, it would be important to note whether they are equally subject to other disturbances. If this were true, it would merely mean that these individuals are more readily affected by many kinds of trauma, including eclamptic poisoning, if you wish to call it that. The speakers have wisely refrained from attempting to state what is the basic cause of eclampsia. All you can say is that this group certainly shows what the Germans call "Minderwertigkeit," a weakness, a vulnerability to the disturbance.

DR. ARTHUR W. BINGHAM.—Dr. Langrock has described cases of patients who are, as we all know, more likely to become toxic, and who are poor risks medically and surgically as well as for maternity. That does not explain, however, the case of the average healthy young woman who eats too much, sits around, and does not exercise, gains too much weight, and develops a disturbance in her metabolism, endocrine glands and water balance. The question is how to prevent toxemia in the average healthy young woman.

A STUDY OF DERMOID CYSTS WITH A SUGGESTION AS TO THE USE OF X-RAY IN DIAGNOSIS*

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SEVENTY-NINE patients with dermoid cysts of the ovary were admitted to the Long Island College Hospital from October, 1923, to May, 1936. Analysis of these cases emphasizes certain features which have considerable clinical significance. The youngest patient was fifteen years of age and the oldest fifty-eight. Sixty-five, or 82 per cent, were observed between the third and fourth decades of life.

Among 500 consecutive ovarian neoplasms removed during this period, dermoid tumors ranked second to the serous cystomas which constituted one-third of our material and, surprisingly, they were more common than the pseudomucinous cysts which were noted in only 9.2 per cent of the cases.

*Presented (by invitation) before the New York Obstetrical Society, November 10, 1936.

the fact that these tumors usually contained a compressed segment of ovarian parenchyma sufficient to maintain the cycle. Marked changes in menstruation accordingly occur only late in the course of the tumor's growth.

COMPLICATIONS

Twenty-one of the specimens were insignificant in size. Only 70 of the tumors studied, therefore, were capable of producing complications, the relative frequency of which is shown in Table II.

TABLE II

	NO. OF CASES	PER CENT
Adhesions	16	23.0
Torsion	15	21.4
Pelvic abscess	1	1.4

As torsion was associated with adhesions in three and in one of these a coincident infection was also observed, 29, or 41.4 per cent, of our patients developed one or more complications. Two small dermoids were found in conjunction with ovarian carcinoma, but these were considered as concomitant findings.

In 16 instances the tumor was adherent to other pelvic organs. Ten of these patients complained of abdominal pain, thus substantiating the statement that abdominal pain occurs most frequently as the result of adhesions. This complication may be produced by the irritating contents of the cyst, and the late Dr. Polak noted that peritonitis was prone to follow intraabdominal rupture of a dermoid.⁵ In one of our patients, rupture during extirpation resulted in the formation of adhesions sufficiently dense to cause intestinal obstruction.

When adhesions develop, the tumor usually becomes fixed to the rectum or the bladder. This favors the transmission of pathogenic bacteria via the lymphatics into the cyst, and the secondary infection thus produced may give rise to a pelvic abscess. In one patient a posterior colpotomy was done for such a pelvic abscess, and the correct diagnosis was made only when teeth were discharged through the colpotomy incision.

TORSION

Dermoids are prone to undergo torsion. The incidence of its occurrence in our clinic as well as in the material reported by other writers is given in Table III.

TABLE III

	NO. OF DERMIDS	NO. SHOWING TORSION
Shaw	23	3
Sänger	33	6
Furlong	50	5
Long Island College Hospital	70	15
Konehy	100	12
Sterer	248	43

The greatest number of twists found in the pedicles of our 15 cases complicated by torsion was six. Free fluid in the abdomen was noted in two. Eleven patients complained of abdominal pain which in four instances was brought on by a change in posture. Four women complained of nausea and vomiting, while three felt a tumor mass. Nine of the tumors which had undergone torsion were in the anterior culdesac, two in the posterior culdesac, one in the right fornix, and only one was in the abdominal cavity. In the remaining two, the location of the tumor was not recorded. These observations are unusual, for torsion is held to be more common

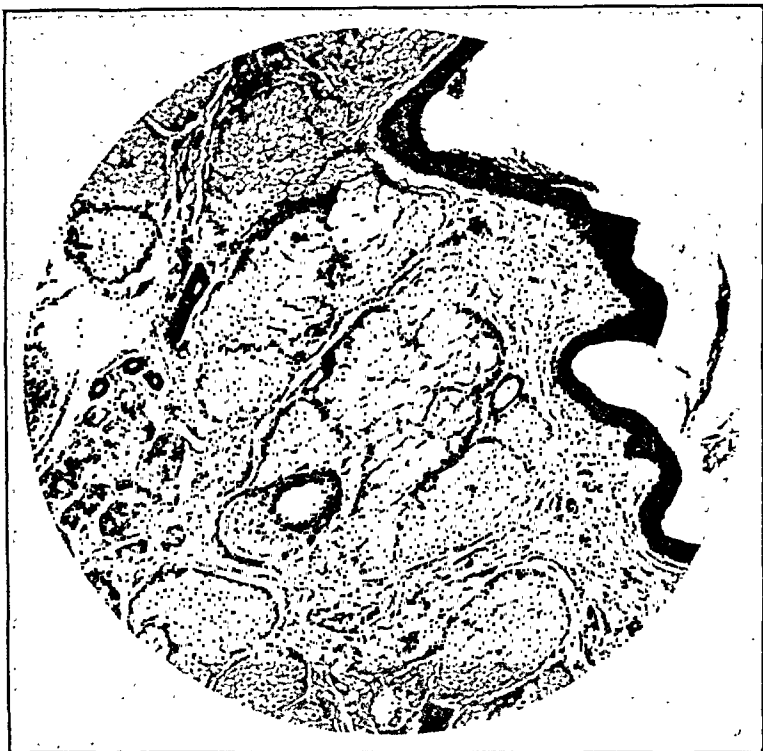


Fig. 1. Section taken through a dermoid anlage presenting adult squamous epithelium beneath which are many cross-sections of sebaceous glands, sweat glands, and hair follicles.

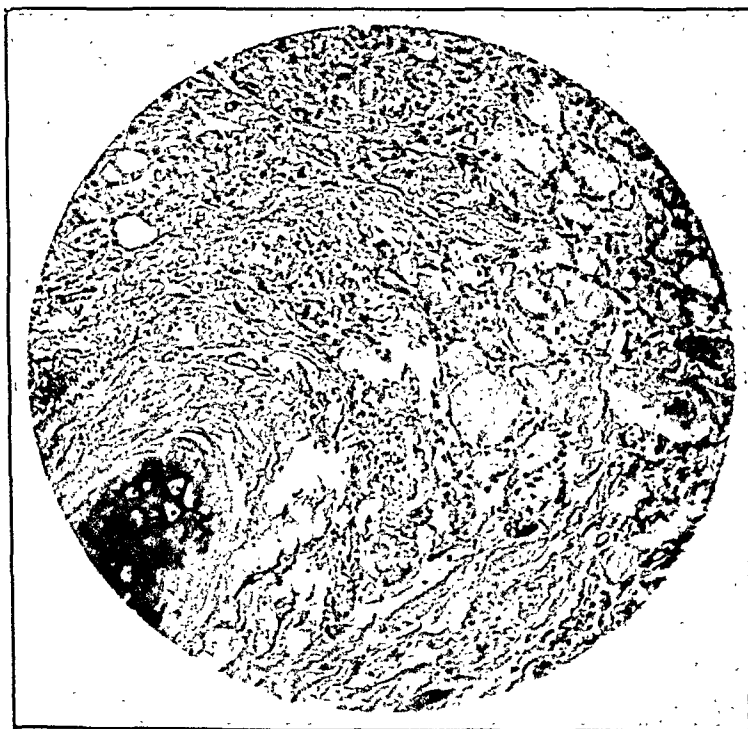


Fig. 2.—This section has been taken through a dermoid cyst, revealing a segment of adult hyaline tissue surrounded with typical thyroid tissue.

remaining cases the preoperative impressions were as follows: Ovarian cyst in 41; fibroid uterus in 21; adnexitis in 7; and in each of the remaining 3, pelvic tumor, hydrosalpinx, and pelvic abscess, respectively, were suspected.

In spite of all that is said to the contrary, a correct preoperative diagnosis should be made more frequently. The vast majority of dermoids are found in the pelvis. In 61 cases where the location was noted, 60 were in the pelvis and only 1 was free in the abdominal cavity. Of those in the pelvis, 39, or 64 per cent, were situated either in the anterior or the posterior culdesacs. The sebaceous material commonly encountered within the locule, intermingled with teeth or bone, produces characteristic areas of pultaceous and solid consistency which are demonstrable on palpation, particularly when the tumor is in the pelvis.

The neoplasms in 39, or 49.4 per cent, of our 79 patients contained calcareous substances, a higher incidence of this finding than is ordinarily reported. Excluding the urinary tract, radiopaque shadows in the female pelvis other than phlebolites, are uncommon, and are due to calcified areas in a fibroid uterus, a lithopedion, calcified lymph nodes, or a dermoid cyst (Fig. 3). According to Dr. A. L. L. Bell, Radiologist of the Long Island College Hospital, a correct interpretation of the shadows due to the calcareous structures within a dermoid cyst can usually be made. We feel that a higher incidence of correct preoperative diagnoses could have been made in our series had the x-ray been used more frequently. We therefore strongly advise the use of the x-ray whenever the anterior position of a pelvic tumor, or its feel on palpation, suggests a dermoid cyst.

TREATMENT

The frequency with which these tumors undergo complications makes it advisable that they be extirpated as soon as the diagnosis is made. Oophorectomy is always indicated in unilateral dermoids. Since 17.7 per cent of our cases showed bilateral involvement, both ovaries should be removed whenever this is not contraindicated by the age of the patient. In a young woman, if the opposite ovary is enlarged, or if a zone of hardness is felt, the organ should be hemisected and searched for a small dermoid locule. Should one be encountered, its enucleation is indicated. Bilateral dermoids are best handled by double oophorectomy. On the other hand, if the patient is young, resection of the ovary least involved may be substituted, a procedure which has been done successfully in a number of cases. The possibility, however, of the usual sequelae of resection must be considered. In this connection, it may be stated that the increasing knowledge of ovarian substitution therapy in artificial menopause makes the decision less difficult.

As a rule the immediate postoperative course was uniformly good and the majority of our patients were discharged from the hospital at the end of fourteen days.

FOLLOW-UP

Four patients in our series died. In two, small dermoids were found in conjunction with ovarian malignancies which caused fatal carcinomatosis seven and twelve months after operation. One patient died three days postoperatively of myocardial failure. The fourth death resulted from cardiac decompensation and bronchopneumonia fourteen days after operation. The corrected mortality is 2.5 per cent.

Our follow-up consists of 61 patients seen ten months to nine years following operation. In short, the pelvic findings and symptoms noted during these examinations are too few and varied to warrant any discussion.

It is significant, however, that 7 patients subsequently have delivered full-term normal infants, and 2 were gravid at the time of their last examination.

in the abdominal rather than in the pelvic phase. The laboratory data were insignificant except in this group, 9 patients of which had a leucocyte count of more than 10,000. In one, the temperature was elevated to 99.6° F.

MALIGNANT CHANGES

Two small incidental dermoids were found in conjunction with ovarian malignancy. One was an embryonal carcinoma and the other accompanied a papillary cyst adenocarcinoma. Neither carcinomatous nor sarcomatous change was present in any of the cases.

DERMOIDS WITH PREGNANCY

Five of our cases were associated with pregnancy. Two presented no symptoms and were recognized for the first time during the initial prenatal examination. The remaining three complained of abdominal pain. One patient experienced a rapid increase in the size of her abdomen though she knew herself to be but three months pregnant. Pregnancy is said to favor torsion in dermoids.⁷ Theoretically, the enlarging pregnant uterus alters the position of the tumor, and as it is elevated into

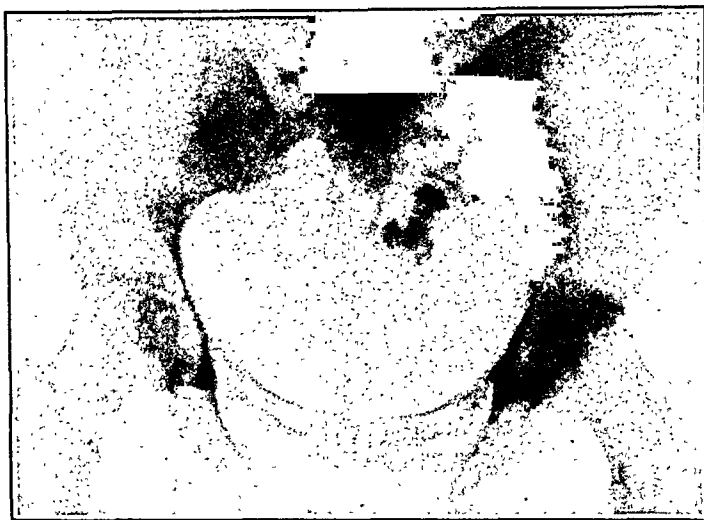


Fig. 3.—X-ray revealing well-formed teeth in the left ovary which is the seat of a dermoid tumor.

the abdominal cavity a twisting of the pedicle may occur. Among our five pregnancy cases, however, the tumor was located in the abdominal cavity above the uterus in but one, while the remaining four were found twice in each of the cul-de-sacs. Complications were noted in three cases. One tumor was twisted, and one covered with adhesions. In the third patient, the tumor was incarcerated in the pelvis in front of the fetal head. A cesarean section was done, because it was felt that labor might rupture the cyst, or the tumor itself might cause dystocia. At operation the head was floating and the dermoid was deeply incarcerated in the pelvis.

Fifty-seven patients had been pregnant one or more times. That sterility is not influenced by dermoids even when they are bilateral has been shown by Manton who collected 19 cases of pregnancy associated with bilateral tumors.

DIAGNOSIS

The diagnosis of dermoid cyst is rarely made (Counsellors). This statement was borne out in Marshall's series where the correct diagnosis was never made with any degree of certainty, though suggested in a few instances. In our group, it was diagnosed seven times and in one, this was the result of x-ray examination. In the

DR. VINCENT P. MAZZOLA.—The following case will emphasize the use of the roentgen ray in the preoperative diagnosis of dermoids, a procedure of particular value in the case of children where the diagnosis of abdominal tumors is difficult.

A child about five years old was admitted to my service at St. Peter's Hospital, complaining of epigastric pain, vomiting, and an abdominal tumor. On examination, she presented a tumor mass about 7 cm. in diameter in the epigastrium. The tumor was semicystic, freely movable and not tender. An abdominal flat x-ray plate was taken which revealed a tumor mass containing opaque substance which resembled rudimentary mandible and teeth. The diagnosis of dermoid cyst was made and confirmed at operation. (Slides showing the gross appearance of the tumor and the roentgenograms before and after removal from the abdomen.)

DR. FRANK R. SMITH.—At the Memorial Hospital we have a rather distorted distribution of types of ovarian tumors. The dermoids formed only about 8 per cent of all ovarian tumors. The distortion is shown by the fact that in 1932, in reviewing a series of 376 patients with ovarian tumors, I found that only 54 were benign. You get a further idea of our distortion when you appreciate that 78 per cent of patients with malignant tumors had been operated upon previously, coming to us after either an incomplete operation or simple exploratory celiotomy.

For some time we have been interested in x-raying certain ovarian tumors, perhaps with the idea of seeing if we could diagnose them as dermoid cysts. Yet even when suggestive shadows were present, some of our guesses have been wrong. Two patients with missed abortion, one with retention of a fetus for twenty years and the other for nine years, were each regarded by at least one x-ray man as having a dermoid cyst.

It seems to me that this is an academic study rather than a practical one, for it is hard for me to conceive of an ovarian tumor that does not require operation. Its only value may be to decide whether a given case is to be referred to a surgical or gynecologic service.

142 JORALEMON STREET

340 HENRY STREET

RUPTURE OF GRAAFIAN FOLLICLES

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(From the Maternity Hospital, Cleveland, and the Medical Department of Western Reserve University)

WHILE doing Friedman tests for pregnancy, the phenomenon of the rupture of the ovarian follicles excites one's interest. We wonder at the mechanism which causes these tiny blebs, after lying almost dormant for the whole life of the female, to swell up and burst within the course of a few hours under the influence of what we call a hormone. We have reported previously the actual observations of this process.¹ The peritoneal cavity of a rabbit was opened nine hours after an injection with the urine of a pregnant woman. The whole cavity was expanded, and filled with warm mineral oil, following the technic of Dr. E. E. Ecker.² At that time, some follicles were already markedly swollen. They increased slowly, until finally the thin area at the stigma ruptured, releasing a trickle of follicle fluid and blood into the surrounding oil. The first follicle ruptured ten hours and twenty-six minutes after the injection of urine.

SUMMARY

1. There were 15.8 per cent of 500 consecutive ovarian tumors which were dermoid cysts.
2. Eighty-two per cent occurred between the third and fourth decades.
3. In 15.2 per cent both ovaries were involved at the time of admission, and two patients previously had the opposite ovary removed for a dermoid, so that 14, or 17.7 per cent, actually had bilateral involvement.
4. In 29 instances adhesions, torsion, or infection were encountered as complications.
5. Five cases were associated with pregnancy. Follow-up also showed that 9 of our patients became pregnant subsequent to a unilateral oophorectomy.
6. The postoperative course and follow-up in the majority of cases were uneventful.
7. The corrected mortality was 2.5 per cent.
8. Teeth or bone, alone or in combination, were encountered in 39, or 49.4 per cent, of our cases. Had x-ray been used more frequently, a high percentage of these tumors could have been diagnosed before operation.

We wish to express our sincere thanks to all the members of the Gynecological Staff for their cooperation and kindly suggestions.

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DISCUSSION

DR. SAMUEL A. WOLFE.—In our series at the Long Island College Hospital we encountered no secondary malignant changes in the dermoid itself. Carcinomas have been described in the epidermoid lining, the frequency being estimated at about 1 per cent.

The clinical problem of bilateral dermoids in young women, particularly those desiring children, is one of great importance. Where there are multiple dermoid locules, it is almost impossible to conserve any segment of ovarian parenchyma, but care and persistence will reveal a segment which can be retained to continue menstruation and fertility.

In our series of dermoids, segments of thyroid tissue were frequently seen on microscopic examination. In two, however, the thyroid tissue practically obscured all other elements, and a diagnosis of struma ovarii was properly made. In both cases the thyroid showed no evidence of secondary malignancy or hyperplasia and signs of thyroid intoxication were lacking.

this cap the capillary glass tube is thrust, as a hypodermic needle is thrust when removing a dose of vaccine from its bottle.

A series of such capillary tubes was set up, using for the central drops salt solutions of known concentration. Notwithstanding some eccentric observations, the increase in droplet size followed the amount of salt in the solution surprisingly. The results are given in Table I. Put on coordinate paper, the horizontal distance repre-

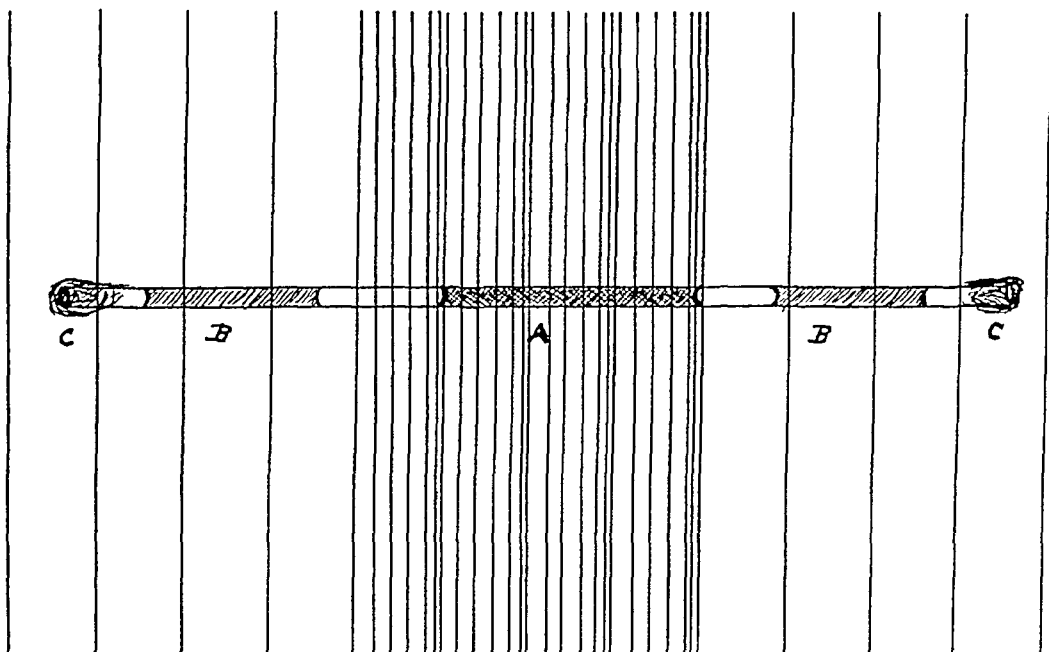


Fig. 1.—Capillary tube, on grating, for measuring length of central drop. (To avoid confusion, cross lines of grating are not shown.) A, Droplet of fluid to be tested. B,B, Distilled water droplets. C,C, Paraffin seals. (Magnification, 1-40.)

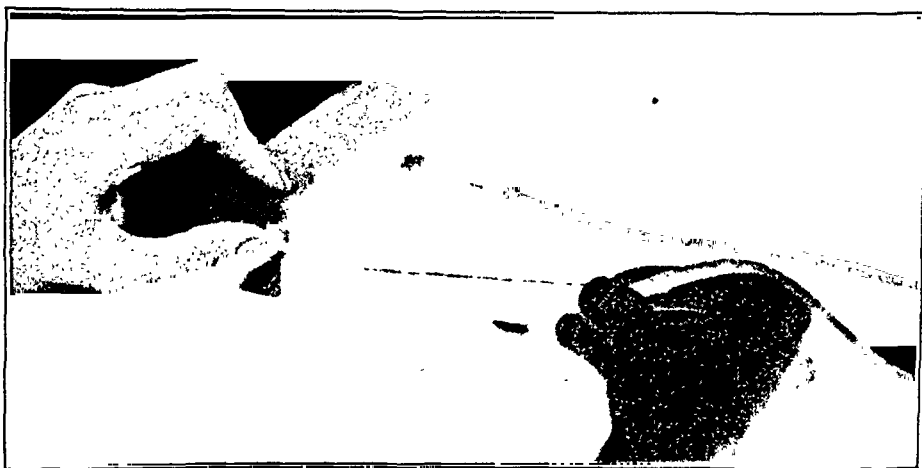


Fig. 2.—Apparatus used to draw fluid into capillary tubes.

sents the *percentage* increase in the drop length, while the vertical distance shows the *percentage* of salt in the central droplet. This is illustrated in Fig. 3. A line run through the mean of the observations at each saline *percentage* tested seems to approximate more to a curve than to a straight line. However, this effect may be a false one caused by the drawing of the curve far to the right on the 0.85 per cent ordinate by a few very erratic observations which are probably incorrect.

Several theories have been proposed to explain this mechanism of rupture.³ We feel that, if we hope ever to understand the action of hormones, an important first step is to find out just what changes they cause in the follicles of the ovary. The formation of the *corpora hemorrhagica* is merely a result of these changes. There are three main theories as to the cause of this rupture:

1. Smooth muscle fibers in the ovarian stroma contract rhythmically, and squeeze the tense follicle. But there is little histologic evidence for the presence of such fibers in the ovary. In our observations under oil, in spite of the closest watching, no sign of motility could be detected in the ovary.

2. An enzyme digests the internal lining of the follicle wall until it is too weak to resist the fluid pressure. There seems to be little direct evidence for this view. On pressure, a follicle about ready to rupture seems fully as tough as does one that has not been stimulated.

3. Increased intrafollicular pressure, due (a) to change in the osmotic tension of the fluid, or (b) to liquefaction of the cells in the so-called bodies of Call and Exner. At the time we observed the follicles under oil, one could not but be impressed by the evidences of increased internal pressure. The follicles swelled up, enlarged, projected above the surface of the ovary, and showed every appearance of being tense. When such a follicle was tapped with a capillary glass tube, the fluid rushed up faster and higher than did the fluid drawn from an unstimulated follicle into a similar tube.

How could the osmotic tension of such a tiny amount of fluid be estimated? After many efforts, we tried a vapor tension method described by Walker.⁴ This was used by White for comparing the molecular concentrations of urine and of plasma in kidney glomeruli. We drew three droplets, separated by air spaces, into a glass capillary tube. The first and third droplets were distilled water. The central drop was the fluid to be tested. Hygroscopic substances present in that central droplet will cause it to take up water from the vapor in the air on each side of it. Thus, such a droplet will increase in length. Rather to our surprise, we found that it actually does so increase to a very measurable extent. As soon as made up, the ends of the tube are sealed with paraffin; and the length of the central droplet is measured, lying upon the grating of a blood corpuscle counter (Fig. 1). The length of the drop is again measured after twenty-four hours. As it proves technically impossible to get the drops in different tubes of exactly the same length, or even to get capillary tubes of exactly the same caliber, the increase in length is expressed in *percentage* of the original length of the droplet. After numerous experiments, it was found possible to fill the capillaries by means of the apparatus illustrated (Fig. 2). The bulb of an eye-dropper, held in a hinged clamp, can be compressed or relaxed accurately with the pressure of a finger. A tube connects the dropper nozzle with a solid rubber cap of a vaccine ampule. Through

TABLE I. CAPILLARY EXPANSION OF DROPS OF VARYING KNOWN CONCENTRATION OF NaCl

PER CENT SALINE	DROP LENGTHS, EXPRESSED IN $\frac{1}{20}$ MILLIMETERS		PER CENT CHANGE
	AT START	AFTER 24 HOURS	
0.85	22	27	plus 22.6
	90	99	plus 10.0
	17	21	plus 22.2
	28	32	plus 14.2
	40	46	plus 15.0
	35	40	plus 14.3
	51	56	plus 9.8
	48	52	plus 8.3
	46	51	plus 10.8
	43	48	plus 11.6
	43	47	plus 9.3
	30	33	plus 10.0
	39	43	plus 10.0
	33	37	plus 12.1
	44	52	plus 20.0
0.76	27	30	plus 11.1
	42	45	plus 7.1
	26	29	plus 11.5
	36	40	plus 11.1
	50	55	plus 10.0
	36	39	plus 8.4
	50	54	plus 8.0
	55	60	plus 9.1
	18	20	plus 11.1
0.68	28	31	plus 10.7
	36	40	plus 11.1
	23	27	plus 13.0
	48	52	plus 8.3
	65	69	plus 6.1
	28	30	plus 7.1
0.59	37	40	plus 8.1
	25	27	plus 8.0
	38	40	plus 5.3
	24	26	plus 8.3
	45	48	plus 6.7
	38	40	plus 5.3
0.51	46	48	plus 4.4
	45	47	plus 4.4
	14	15	plus 7.1
	62	65	plus 4.8
	31	33	plus 6.4
0.42	23	24	plus 4.3
	28	30	plus 7.1
	38	40	plus 5.2
	43	45	plus 4.6
	40	42	plus 5.0
	49	51	plus 4.1
	40	42	plus 5.0
	50	53	plus 6.0
	48	50	plus 4.1
	58	60	plus 3.4
0.34	25	26	plus 4.0
	48	50	plus 4.2
	53	54	plus 1.9
	48	50	plus 4.1
	37	39	plus 5.3
	43	45	plus 4.6

After this curve had been estimated, the next step was to take fluid from swollen, but not ruptured, graafian follicles of rabbits ten hours after they had been injected with the urine of a pregnant woman. At the same time, to avoid any differences that temperature changes might cause, capillary tubes were also set up containing fluid from mature follicles that had not been stimulated by injection. In taking these droplets, the greatest care must be exercised lest the glass tube

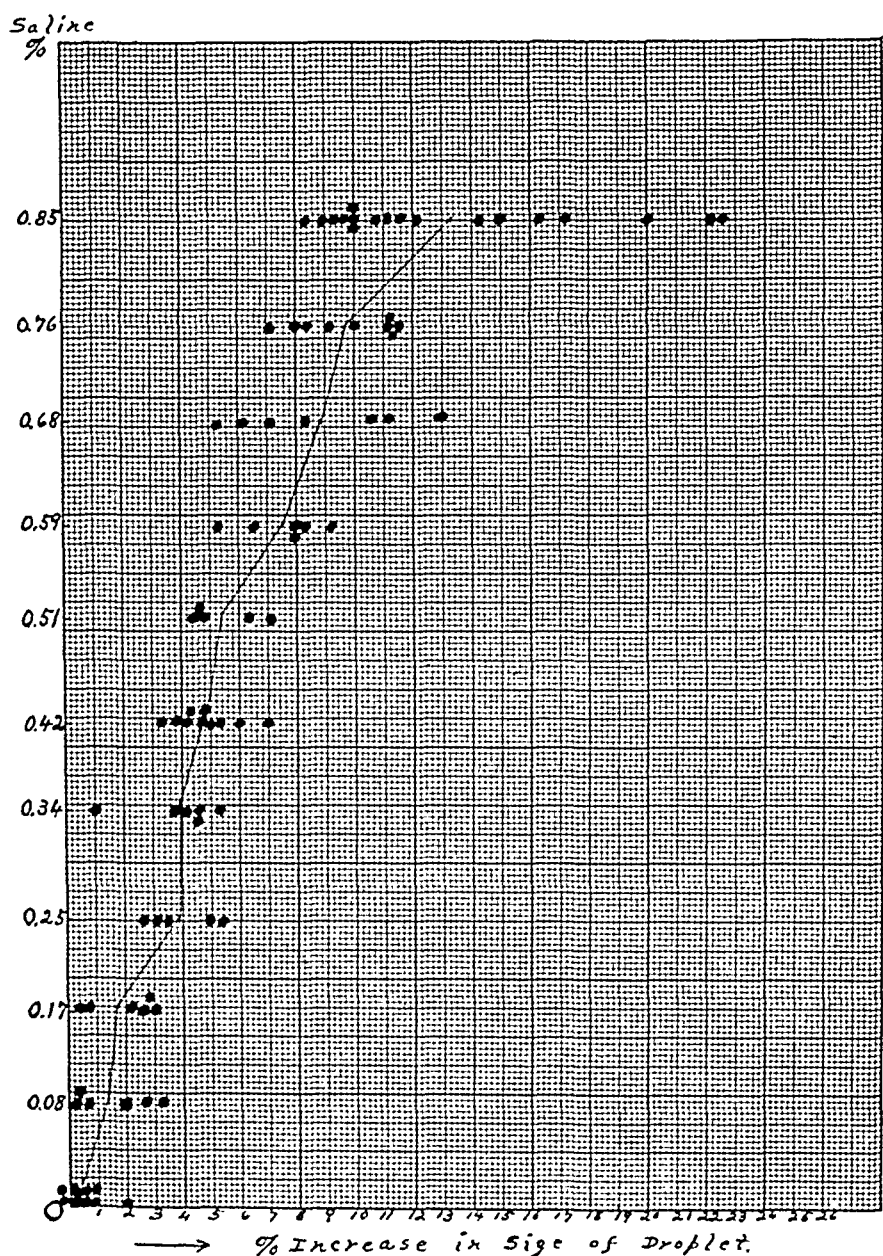


Fig. 3.—Expansion of droplets of known concentration of NaCl.

penetrate too far into the tiny follicle, injure the capillary bed on the under-side, and contaminate the fluid with blood. There certainly was a definitely different, if slightly erratic, rate of lengthening in the two sets of droplets. Table II shows the results.

We have drawn on coordinates the same curve we derived from the means of the salt drops of known concentration. On this curve, we have interpolated the results from the observations on the follicle droplets, where their rate of expansion line

in our observations. However, we are convinced that there is a very real difference in the response of the two types of follicle fluid to these experiments.

If the chloride content of blood plasma is 0.64 per cent, and the total inorganic content is 0.85 per cent, a solution such as our stimulated

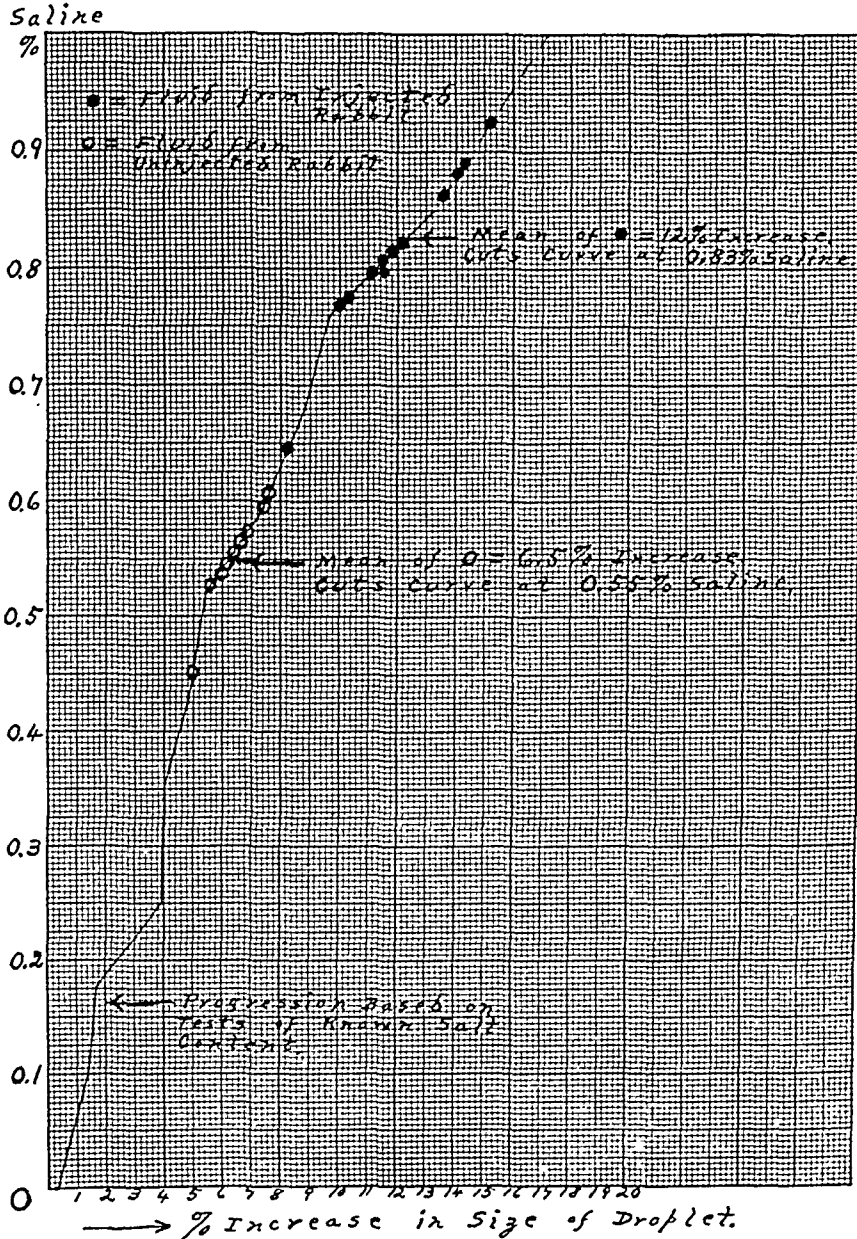


Fig. 4.—Expansion of droplets of ovarian follicle fluid (rabbit).

follicle fluid, having a content of hygroscopic substances amounting to 0.83 per cent, would be hypertonic. For not all of the inorganic plasma content is hygroscopic. For example, 0.044 is oxygen. Certainly the fluid from a nonstimulated follicle is decidedly hypotonic if its salt content is only about 0.55 per cent.

TABLE I—CONT'D

PER CENT SALINE	DROP LENGTHS, EXPRESSED IN $\frac{1}{20}$ MILLIMETERS		PER CENT CHANGE
	AT START	AFTER 24 HOURS	
0.25	35	36	plus 2.8
	54	56	plus 3.7
	32	33	plus 3.1
	35	37	plus 5.7
	40	42	plus 5.0
0.17	45	45	0.0
	46	46	0.0
	37	38	plus 2.6
	33	35	plus 3.0
	35	36	plus 2.8
	37	38	plus 2.6
0.08	43	43	0.0
	35	36	plus 2.8
	25	25	0.0
	29	30	plus 3.4
	30	30	0.0
	48	49	plus 2.0
Distilled water	49	49	0.0
	50	51	plus 2.0
	108	109	plus 0.9
	40	40	0.0
	43	43	0.0
	46	46	0.0
	24	24	0.0

intersects that curve. The result is expressed in Fig. 2. On this curve, we note the mean of the observations on the fluid from stimulated follicles, and also the mean of the nonstimulated *liquor folliculi*.

Such reasoning would lead us to think that the fluid of a follicle just ready to burst has an osmotic tension equal to a solution of NaCl of 0.83 per cent; while fluid from an unstimulated follicle is equivalent to a 0.55 per cent salt solution. We would be the first to admit that such fine-drawn conclusions are not justified by the wide limit of error

TABLE II. EXPANSION OF FOLLICLE FLUID (RABBIT) IN CAPILLARY TUBES

INJECTED RABBIT LENGTH OF DROP			UNINJECTED RABBIT LENGTH OF DROP		
START	END	PER CENT CHANGE	START	END	PER CENT CHANGE
59	66	plus 11.9	13	14	plus 7.7
22	25	plus 13.6	47	50	plus 6.4
28	32	plus 14.3	47	50	plus 6.4
50	56	plus 12.0	29	31	plus 6.9
38	42	plus 15.2	20	21	plus 5.0
35	39	plus 14.3	40	43	plus 7.5
49	53	plus 8.2	45	48	plus 6.7
70	78	plus 11.4	18	19	plus 5.6
45	50	plus 11.1	50	53	plus 6.0
68	75	plus 10.3			
10	11	plus 10.0			
44	49	plus 11.4			

THE RELATIONSHIP BETWEEN INFECTED URINE AND THE ETIOLOGY OF PYELITIS IN PREGNANCY

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THE objectives of this investigation were to determine: (1) The incidence and character of bacteriuria of the bladder as compared with that of the ureter in normal antenatal and postnatal women, and (2) the etiologic significance of these to pyelitis of pregnancy.

Theoretical and Historic Considerations.—It is generally believed that the urine of normal pregnant women near term is frequently infected with *Bacillus coli* and occasionally with other microorganisms such as streptococci and staphylococci, without producing inflammation of the bladder or upper urinary tract. This concept, frequently referred to as the *bacilluria of pregnancy*, has been applied particularly to bladder urine, but it has also been advanced for ureteral and kidney urine as well. To explain the presence of the *Bacillus coli* in the urine of the upper tract many writers (Zangemeister, Posner, Boeda, Cathala, Bar) have postulated that this organism is excreted by the kidney under certain conditions, most prominent among which they mention pregnancy. They therefore emphasize this possibility as a means of accounting not only for the presence of microorganisms in these locations, but also for the higher incidence of pyelitis and ureteritis in the gravid woman. On the other hand, other observers express a different point of view, stating that the bladder urine, particularly near term and in the puerperium, becomes infected from the urethra, and that the ureteral urine is secondarily involved in an ascending manner, probably being regurgitated through incompetent ureterovesical valves. A third group (Kretschmer, Dudgeon, Williams, Smith, Luys, Le Fur) has been unwilling to accept either of these explanations of the route of infection and has preferred to believe that the lymph stream is primarily responsible, supposing that it brings organisms, particularly *B. coli*, from the bowel, the gallbladder, the vagina or bladder to the upper portions of the urinary tract, where they multiply and frequently attack the walls of the kidney pelvis and ureter. We are lacking in the elements of evidence necessary to establish any of these theories upon a firm basis, so that the preventive and curative treatment of urinary tract infections complicating pregnancy have necessarily been based upon empirical foundations rather than those of a more definite and specific nature. It is the purpose of this

On the basis of these observations, therefore, we think there is evidence that graafian follicles enlarge and burst because the osmotic tension of the fluid is increased.

The profession is thinking much at present about the theory that some toxemias of pregnancy are caused by the great increase in the amount of circulating hormones at such times.⁵ We are also thinking of Arnold's⁶ teaching that edema and upset salt balance are the outstanding features in eclampsia. Can there be a hormone influence that causes an edema of a follicle in a Friedman test, and also a generalized edema of the eclamptic's body when present in excess? We hope to follow along this path with further observations in the near future.

SUMMARY

The phenomenon of rupture of the graafian follicles is discussed, and the theories of its mechanism are mentioned.

A method of testing the hygroscopic content of follicle fluid, based on vapor tension, is described.

CONCLUSIONS

Fluid from a rabbit ovarian follicle just about to rupture after the animal has been injected with urine from a pregnant woman has an osmotic tension somewhere near that of a solution of salt of 0.83 per cent.

Fluid from follicles of unstimulated rabbits has an osmotic tension equal to that of a salt solution of about 0.55 per cent.

I wish to express my gratitude to Dr. Arthur H. Bill for help and suggestions in pursuing this work.

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10515 CARNEGIE AVENUE

Toeroek, G., and Neufeld, L.: Vitamin C Deficiency During Pregnancy, Klin. Wchnschr. 15: 417, 1936.

The authors describe a new biologic method for the determination of the amounts of vitamin C present during pregnancy. They examined 75 women during pregnancy and found that 16 or 21.3 per cent had a definite vitamin C deficiency. During the next ten days these women were given 350 mg. of ascorbic acid which resulted in a complete disappearance of the vitamin C deficiency. Since vitamin C is especially necessary to the pregnant woman during the course of the pregnancy and labor (with special reference to hemorrhage, immunity, etc.), the authors feel that vitamin C therapy is indicated in pregnancy. This is especially important during the winter months.

RALPH A. REIS.

Duncan and Seng in 1928 studied 42 normal pregnant women with the following results:

	ANTEPARTUM		POSTPARTUM	
	RIGHT URETER	LEFT URETER	RIGHT URETER	LEFT URETER
W.B.C.	23.0%	9.0%	8.0%	11.0%
Pus	0.0%	2.4%	2.7%	2.7%
Coliform organisms	9.0%	9.0%	2.7%	11.0%
Cocci	50.0%	35.0%	61.0%	39.7%
No growth	56.0%	47.0%	36.0%	63.0%

The high incidence of cocci in this report leads to the inference that there may have been many contaminants. Taking only the positive *B. coli* cultures as a criterion, one may conclude that there were approximately 9 per cent of true ureteral urine infections in their antepartum and 11 per cent in the postpartum patients.

Such data, and the fact that there are no others of importance available, give the impression that the bacteriology of the upper urinary tract in pregnant women needs further study, for it is extremely difficult to account for the high incidence of 70 per cent of infected urine found by Albeck, or even 59 per cent as reported by Duncan and Seng, when it is remembered that not more than 2 per cent of pregnant or puerperal women develop clinical pyelitis. If, on the other hand, they do present an accurate bacteriologic estimate of the upper urinary tract of the pregnant woman, they should be confirmed. Therefore, an investigation of the bacterial content of bladder and ureteral urine in the normal pregnant woman has been planned and carried to completion.

METHOD AND APPROACH TO PROBLEM

Thirty normal gravid patients were repeatedly observed with respect to the bacterial content of the urine secured from the bladder and ureter at various stages of antenatal and puerperal periods.

In obtaining the ureteral specimens, the water cystoscope was used, the right ureter catheterized and the catheter passed well up to the ureteropelvic junction. After allowing the first ten drops of urine to escape, the tip of the catheter was flamed and five drops of urine were allowed to fall directly on an ascitic-agar slant. Several drops were then taken for microscopic examination. The agar slants were incubated and reported negative at the end of five days if no growth was present. If growth occurred, subcultures were made and the organisms classified by cultural and fermentation methods.

It was hoped that by collecting the urine directly on the agar slant rather than by transferring it from a sterile tube to a slant or to broth culture medium, it might be possible to reduce contamination to a minimal degree, as well as to obviate the possible death of organisms which might result from delayed transfer to culture media and the incubator.

The bladder cultures were made just prior to each cystoscopic examination. The bladder was catheterized with a sterile glass catheter

paper to present evidence concerning the incidence of bacilluria in normal pregnancy which, we believe, tends to support the theory that the lymphatics of the bowel and pelvis transmit the *Bacillus coli* to the urinary tract in the pregnant woman, as well as to point out a few of the means which may be adapted to the antenatal care of women which will tend to reduce the incidence of pyelitis of pregnancy.

In the past there have been numerous studies of bladder urine, all of which have seemed to demonstrate beyond doubt that the urethra and bladder are often infected in late pregnancy and the puerperium, and further, that this can occur with no manifestations of cystitis or ureteritis.

Albeck (1907) made the first extensive survey, the results of which supported this point of view. Since Albeck's report, many others have studied the bladder urine and have more or less definitely verified his findings. Of such reports one should mention the following: Duncan and Seng (1928) found the urine infected in 42 per cent of their antepartum and 80 per cent of their postpartum patients; Crabtree and Prather (1930) reported a much lower incidence in antepartum women, namely 13 per cent; while in more recent reports, Harris and Herrmann (1936) found that 74 per cent of their antepartum and 94 per cent of their postpartum patients had bacilluria, and both Dodds and Baird, who studied very large numbers of women, found an incidence of infected bladder urine of 6.8 per cent.

That a bacteriuria of the bladder occurs in many antepartum women near term cannot be doubted. However, the wide disparity between the findings of Duncan and Seng, and Harris and Herrmann on the one hand, and those of Crabtree and Prather, Dodds and Baird on the other, leaves one in much doubt as to the actual frequency of its occurrence. It would seem necessary that further studies be made with the most careful technic possible before a definite conclusion may be justified.

Infections of bladder urine are of importance because of the possible extension of such infection from the bladder to the ureter and then to the kidney. Therefore, studies in which both the bladder urine and that of the upper tract are taken into consideration are of particular significance in any attempt to evaluate the etiology of upper urinary tract infections in the gravid woman. There are surprisingly few observations of this nature in the literature.

The first was that of Albeck, whose findings in 30 patients are as follows:

Thirteen patients in the first half of pregnancy:

BLADDER URINE		RIGHT URETER	LEFT URETER
Coli infection	10	3	3
Staphylococcus	2	1	1
Streptococcus	1	0	0
Sterile	0	9	9
Bladder urine infection	84%	Ureteral urine infection 23%	

Seventeen patients in the last half of pregnancy:

BLADDER URINE		RIGHT URETER	LEFT URETER
Coli infection	17	12	15
Staphylococcus	0	0	0
Streptococcus	0	0	0
Sterile	0	5	2
Bladder urine infection	100%	Ureteral urine infection 70%	

presence of streptococci in the bladder and its absence in the ureter is also taken as strong evidence against the regurgitation theory of ureteritis.

The total uncorrected incidence of positive cultures from kidney urine is therefore 12 per cent; for *B. coli* alone, it is 0.86 per cent; and for pathogenic organisms, if contaminants and nonpathogens are eliminated, it is 1.73 per cent. *B. coli* was found in the bladder urine seven times, giving an incidence of 6.08 per cent for vesical colibacilluria. Table I. sets forth these findings in more complete form.

TABLE I .

	ANTEPARTUM				POSTPARTUM			
	FIRST HALF		SECOND HALF		FIRST 14 DAYS		LATER	
	BLAD- DER	RIGHT URETER	BLAD- DER	RIGHT URETER	BLAD- DER	RIGHT URETER	BLAD- DER	RIGHT URETER
<i>B. coli</i>	1	0	5	0	2	0	0	1
Streptococcus	11	0	18	0	5	0	1	0
<i>Staphylococcus</i> <i>albus</i>	14	1	22	1	5	1	3	1
Chromobacterium	0	1	1	6	0	0	0	0
Diphtheroids	5	0	6	1	1	0	0	0
Lactobacillus	2	0	2	1	0	0	0	0
No growth	8	26	18	50	4	10	10	15
	41*	28	72*	59	17*	11	14*	17

*More than one microorganism was recovered from individual bladder cultures on several occasions, which accounts for the discrepancy between the total numbers of bladder and ureter cultures in each group.

Thus it will be seen that the results of this investigation are in close agreement with the reports of Dodds and Baird as regards *bladder urine*, their reported incidence of *B. coli* infection being 6.8 per cent as compared with the 6.08 per cent incidence of this study. There is marked disagreement, however, with the other observers who have found an incidence of from 13 per cent to 94 per cent. It would appear that their methods were faulty or their choice of patients such as to give an excessively high number of positive cultures.

As regards infection of *ureteral urine*, on the other hand, the comparison of results is as follows:

		RIGHT URETER
Albeck	{ <i>B. coli</i> infection	50.00 per cent
	{ Total positive cultures of all organisms	51.00 per cent
Duncan and Seng	{ <i>B. coli</i> infection	11.00 per cent
	{ Total positive cultures of all organisms	50.00 per cent
Present study	{ <i>B. coli</i> infection	0.86 per cent
	{ Total positive cultures of all organisms	12.00 per cent

A perusal of these figures indicates that in the 30 women studied the incidence of infection of the ureteral urine was much less than that observed formerly in supposedly similar groups of pregnant women.

after the urinary meatus had been cleansed and the urine collected in a sterile test tube. The bladder urine was then examined microscopically without centrifugalization and cultures made at once in beef infusion broth.

With the above technic, 30 pregnant women have been followed in the prenatal and postnatal periods, repeated examinations being carried out on the majority of them. During the study, the right ureter was chosen for observation, as this tract possesses a marked predilection toward the development of pyelitis, and by thus studying it intensively, it was hoped that the greatest possible incidence of urinary infection might be obtained. The catheter was passed into the ureter 115 times during the pregnancies of these 30 women, with subsequent examination of the urine thus obtained by microscopic and cultural methods. Seventeen patients were catheterized three or more times, six were catheterized seven or more times, and ten on only one occasion. None of the 30 patients developed clinical pyelitis or cystitis.

Of the 115 observations thus made possible, 101 specimens of urine were negative in bacteriologic culture media; 7 proved to contain chromobacterium; 4 *Staphylococcus albus*; 1 diphtheroid; 1 lactobacillus, and only 1 *Bacillus coli*. The single positive culture for *B. coli* was obtained one month postpartum from a patient who had one subsequent postpartum and four antepartum cultures with no growth of organisms. It is interesting to note that in this instance *B. coli* was found in the bladder urine of this patient, whereas it had not been discovered previously, nor was it found in the bladder subsequently.

The same type of organism was not isolated twice from any single patient, while only four women had positive cultures on two occasions, none of the latter being on consecutive examinations. It was thought that the four positive cultures of *Staphylococcus albus* were due to contaminations. The chromobacterium and lactobacillus are definitely non-pathogenic, never having been reported as a cause of urinary tract infection, and moreover, in this study, were not found in the bladder cultures at the same time that they were isolated from the kidney urine. The diphtheroids are considered by some writers to be pathogenic. However, they have never been recovered as the sole infective organisms in pyelitis. In the one instance in which they appeared in this series, the patient had previous and subsequent negative cultures. Although the streptococcus, both aerobic and anaerobic, was found on 35 occasions in bladder urine, it was not demonstrated in any cultures of ureteral urine. One cannot explain its presence in the bladder on the basis of contamination, resulting from the technic used in collecting the specimens, for were this true, it should also have been found in the ureteral urine cultures. It is therefore assumed that like the colon bacillus the streptococcus enters the bladder by way of the urethra in the majority of instances. The

CONCLUSIONS

1. Colon bacillus infection of the urine of normal pregnant women is not as frequent as former reports indicate.
2. The incidence of colibacilluria of the bladder was found to be 6.08 per cent, of the right ureter 0.86 per cent.
3. No evidence was found to substantiate the theory that the kidney excretes microorganisms during pregnancy.
4. No support for the regurgitation theory as to the origin of ureteritis was found.
5. Repeated catheterization of the ureter may be carried out in the pregnant woman without danger of introducing infection, if careful aseptic technic be observed.
6. The view is expressed, with some reservations, that colon bacillus infection of the urinary tract in pregnant women probably occurs by way of the pelvic and abdominal lymphatic stream with transference of microorganisms from the large bowel, etc., to the vicinity of the kidney and ureter.
7. Emphasis is placed upon the hygiene of the large bowel and urinary tract, as well as the importance of ruling out chronic infections as an essential part of prenatal care of pregnant women.

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111 EAST EIGHTIETH STREET

Wobker, Walter, and Ranft, Wolfgang: The Treatment of Pruritus Vulvae With X-Ray, München. med. Wehnschr. 31: 1275, 1936.

Wobker and Ranft present the results obtained with roentgenization in 30 patients afflicted with primary or essential pruritus vulvae. Cure occurred in 8, improvement in 15, while 7 showed no improvement whatsoever.

C. E. PROSHEK.

While the number of observations is too small to permit of absolute conclusions, it is sufficiently large to suggest that additional investigations may greatly modify prevailing conceptions as to the frequency of infection of the urine of the upper tract in normally pregnant women, as well as to confirm a fairly low figure for the incidence of bladder bacilluria.

Many of the patients studied developed the usual dilatation of the ureter characteristic of pregnancy, and a few of the multiparas had cystocele, so that presumably the group was a fairly representative one with respect to retardation and embarrassment of the urinary flow.

It would seem, therefore, that the conception of the normal gravid woman's urinary tract as one beset by numerous microorganisms, particularly *B. coli*, is incorrect and should be modified. Moreover, it would appear that the theory of excretion of bacteria by the kidney lacks substantiation. If this ever occurs in the normal woman, it must be a transitory phenomenon; certainly it cannot be regarded as a usual accompaniment of the pregnant state.

The regurgitation of infected urine from the bladder into the ureters was not demonstrable in any of these patients, for only once in 115 simultaneous observations of bladder and ureteral urine was the same organism recovered from both fields, although as stated above, several of the patients obviously had some degree of stasis of bladder and ureteral urine.

That urinary stasis plays a major rôle in explaining the etiology of pyelitis and ureteritis in pregnancy is unquestionable. This has impressed everyone who has made a study of this disease syndrome. However, stasis alone does not produce the disease. The portal of entry of the chief microorganism concerned, *Bacillus coli*, has not been satisfactorily clarified. From investigations such as this, it becomes more and more apparent that bacillary access into the ureter and kidney pelvis is, in all likelihood, not from the urinary tract itself in most instances, but is probably to be found in the lymph stream and then only when there is disease or stasis in other organs of the lower abdomen and pelvis which harbors the colon group of microorganisms.

From a practical point of view, these conclusions should indicate the importance of thorough elimination through the bowel, as well as the investigation of chronic appendicitis, chronic cervicitis, and chronic cystitis in the pregnant woman, as a preventive form of antenatal care to reduce the incidence of urinary tract infection due to the coliform organisms. In addition, the thorough flushing of the urinary tract by the ingestion of fluids will accomplish much in preventing these organisms from producing local inflammatory processes when they gain entry into it.

multiparas; of the multiparas 7 were para ii. However, as the ratio of primiparas to multiparas delivered on our service is about 2:5, this may indicate that the condition is slightly more common in primiparas.

F. Type of Pelvis.—White and Rucker make as a differential point that retraction ring occurs in obstructed labor due to contracted pelvis or some mechanical obstruction, but that in labor complicated by the development of a contraction ring there is no disproportion between the pelvis of the mother and the presenting part of the fetus.

In our series, the diagonal conjugate was measured in 26 patients and found to be 11 cm. or more in 22 cases. In the remaining 10 cases the diagonal conjugate has been assumed to be normal in 6 patients, as they were multiparas and had had normal deliveries previously. In other words 28 patients or 78 per cent may be considered as having a normal diagonal conjugate. Four primiparas were not measured and four patients were typed as having either generally contracted or flat pelvises.

G. Length of Labor.—The average length of the first stage of labor in primiparas is usually given as sixteen hours, in multiparas eleven hours; of the second stage in primiparas one and three-fourths hours, in multiparas three-fourths hour. In labors complicated by contraction ring both stages are prolonged. In our series Table I will illustrate.

TABLE I

	FIRST STAGE	SECOND STAGE
Primiparas	5½ hr. to 77½ hr.; av. 30.0 hr.	½ to 24 hr.; av. 4¼ hr.
Multiparas	3½ hr. to 32 hr.; av. 17.9 hr.	½ to 8 hr.; av. 3½ hr.

Falls cites lengthened labor as a factor in producing contraction ring but it may be rather that contraction ring prolongs labor.

H. Analgesia.—It is the custom on this service to give all patients in labor sufficient analgesia to make labor quite bearable. In this series of 36 cases (excluding 5 cases sent in by private doctors after attempts at delivery elsewhere with no records as to the analgesia), 9 received no analgesia or only light chloroform analgesia late in second stage, 7 (each a primiparturient) received Gwathmey analgesia, 6 received morphine sulphate once or more, 5 received morphine sulphate and barbiturates, 3 received barbiturates only, and 1 received morphine sulphate and scopolamine.

This amount of analgesia compares with that usually given in labor. Many patients, particularly those of the so-called "neurotic" type, have received considerably more analgesia than any of the above. The staff and nurses do not recall any case of contraction ring developing in a "neurotic" individual.

I. Premature Rupture of Membranes.—This condition is given as an etiologic factor by several authors although in our series it does not appear to be a constant factor as Table II shows.

TABLE II

Prematurely (2 hr. to 3 days before onset of labor)	9 cases or 25.0%
During first stage (cervix dilated 4 cm. or more)	5 cases or 14.0%
At complete dilatation of cervix	15 cases or 41.6%
Not recorded	7 cases or 19.4%

J. Intrauterine Manipulation and Rectal Examinations.—Some consider that contraction ring develops because of intrauterine manipulations. On this obstetric service most parturients are examined and diagnosed by rectal and abdominal

CONTRACTION RING DYSTOCIA

AN ANALYSIS OF THIRTY-SIX CASES, WITH OBSERVATIONS ON THE USE OF ADRENALIN IN TWENTY CASES

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DYSTOCIA due to a contraction ring is a rather uncommon complication in labor. This article is based on 36 cases diagnosed during 14,080 deliveries on the Obstetrical Service of the Louisville City Hospital between Jan. 1, 1926, and Sept. 30, 1935, inclusive, an incidence of one in 391 labors. Only those cases in which the contraction ring was palpated by a member of either the attending or resident staff are included. Twenty cases since Jan. 1, 1931, have been treated by hypodermic injection of adrenalin; sixteen cases prior to that time were treated by other methods.

Several factors have been considered with the object of noting any common condition in all or most of our cases:

A. Menstrual Irregularities.—Onset, cycle and amount of flow are noted in the histories.

Normal menstrual history	25 or 70.0%
Slight irregularities	5 or 13.5%
Gross irregularities	2 or 5.5%
Not recorded	4 or 11.0%

Menstrual irregularities do not appear to play a part in the condition. Probably this may be interpreted as denoting that the contraction ring is not due to endocrine disturbance.

B. Toxemia.—Toxemias as revealed by elevated blood pressure seem to have no bearing on the etiology of contraction ring. In this series 6 patients had systolic pressures of 130 mm. Hg or over and of these only 3 were over 150 mm. Hg at any reading during pregnancy or labor. These 3 patients had diastolic pressures of over 90 mm. Hg, two being admitted with eclampsia.

C. Syphilis.—The blood Wassermann reaction was positive in 6 cases, 2 other patients who were negative at time of delivery had been treated previously; the blood Wasserman was not done in 5 cases, and was found to be negative in 23 or 66 per cent.

D. Age.—Harper found all patients between twenty-four and thirty-six years of age; Michael found the average age of 44 patients to be 33.4 years. In our series the youngest patient was fourteen years, the oldest forty-five years, with an average of 24.3 years. Age seems to play no part in producing a contraction ring.

E. Parity.—Gilliat found in his series of 14 patients that 85 per cent were primiparas. All of Hicks' 5 patients were primiparas. Michael and Harper noted the condition in equal numbers of primiparas and multiparas. White found the condition twice as common in multiparas. In our series 17 were primiparas, 19

perusal of the records there are some cases which suggest the presence of retraction rings found in obstructed labor. The grim picture painted by Falls was seen; "The mother is usually much exhausted, often has a degree or two of fever, and a pulse of 110 to 130. The membranes are usually ruptured and infection of the uterus may be taken for granted, especially if numerous vaginal examinations have been made, as is usually the case, and if there have been previous attempts at operative delivery." Four of our six deaths occurred in these cases.

A contraction ring may continue for an indefinite period. In one of our patients, it was found still present twenty-four hours after first being diagnosed, the uterus continuing to contract rhythmically all that time. In our last patient the ring was again palpated three hours after being diagnosed, and during that time the pains continued regularly. In only one of our patients was the ring noted to have relaxed, and the patient, two hours after being given caudal block and adrenalin, delivered spontaneously.

PREVENTION

Inasmuch as no common etiologic or concomitant factor has been noted, except malpresentation, any rational preventive seems lacking. Since occipitoposterior positions were found in 70 per cent of cases, correction of these positions should be attempted by external manipulations and/or favorable positions of the patient in labor. Of course, the patient should be given supportive treatment to obviate the exhaustion of long labor.

ACTION OF ADRENALIN

Rucker, in 1925, in researches on the action of adrenalin on the uterus found that adrenalin injected subcutaneously inhibited contractions of the uterus for from nine to thirty minutes after the injection. In 1927 he reported two cases in which he used adrenalin subcutaneously with caudal block to relax a contraction ring successfully. Since that time many cases have been reported. Rucker, in discussing the action of adrenalin on the uterus, works out the following rationale of treatment:

1. The uterus is innervated by sympathetic and parasympathetic nervous systems.
2. The sympathetic system probably acts as an inhibitor of uterine action.
3. Adrenalin, the sympathicomimetic hormone, inhibits uterine contractions and thus, rationally, should relax a contraction ring.

(Apropos of this action of adrenalin on the uterus, might the poor contractions of the uterus in women who are much frightened in labor, be due to an excess of adrenalin in the blood resulting from fear?)

Adrenalin also relaxes a retraction ring, but this does not remove the cause of dystocia.

In our series of 36 cases, there were 16 patients treated prior to the use of adrenalin. These 16 patients were, all but one, treated by deep

examinations only, until prepared for delivery. In the patients developing contraction ring, there was an average of 4 rectal examinations in each case and this is not out of the ordinary. Vaginal examinations were *not* done before the patient was prepared for delivery in 21 cases. In patients with slow or no progress, vaginal examinations were made. During labor one vaginal examination was done in 2 cases, 2 vaginal examinations in 3 cases and 3 or more vaginal examinations in 10 cases; but of these 10 cases, 5 patients were sent in to the hospital after attempted deliveries elsewhere. In 3 of the patients in whom vaginal examinations were done, intrauterine manipulations were performed for the insertion of Voorhees' bag, and this was done before the contraction ring was diagnosed.

Of course vaginal examinations were made frequently *after* the diagnosis of contraction ring but these cannot be considered as causative factors.

Since intrauterine manipulations or vaginal examinations were only done in 42 per cent of these cases, it does not appear that such examinations are etiologic factors.

K. Malpresentations.—The only constant finding which might be interpreted as an etiologic factor was malpresentation in practically all of our cases. Only one case is recorded as presenting in L.O.A.; one presentation is not recorded. Thirty-four patients (94.4 per cent) showed abnormal presentations:

LOP	13 cases or 36.0%
ROP	12 cases or 33.3%
(Cephalic presentation)	25 cases or 69.3%
Breech	5 cases or 14.0%
Transverse	4 cases or 11.0%

Obviously this may be only a concomitant condition instead of an etiologic factor, or in other words, since we do not know the cause of malpresentation the same factor may be in effect to cause both conditions.

L. Other Conditions.—Twenty-seven women had visited the prenatal clinic during pregnancy, and nine were first seen in labor. There were 17 white and 19 colored patients. These conditions usually obtain on this service.

DIAGNOSIS

The diagnosis of contraction ring was made by palpation of the ring vaginally in all our cases. It is the rule in this department to investigate the cause of delay after the cervix has been completely dilated one and one-half hours in primiparas and one hour in multiparas, and if the delay is considered due to uterine inertia to apply low forceps. In 6 cases low forceps were applied and when moderate traction did not effect delivery, further examination revealed a contraction ring around the neck of the fetus. Contraction ring was encountered in 5 cases in which version was attempted. In three cases a contraction ring was found around the neck preventing the descent of the after-coming head in breech extraction. In our last three cases on vaginal examination the cervix was found fully dilated, and hanging like a "cuff" around the head of the fetus, while the uterus continued to contract and relax rhythmically, but a thick rubbery contraction ring was found around the neck of the fetus.

Several writers do not make any differentiation between contraction and retraction rings, and in our records none is made, but on careful

In our series of 36 cases, there were six maternal deaths. Four women died shortly after delivery, three of them having ruptura uteri. The remaining two died on the ninth and tenth days postpartum of bronchopneumonia and puerperal sepsis, respectively. Since the use of adrenalin, beginning January, 1931, there have been no deaths from sepsis and two maternal deaths from ruptura uteri, one patient being admitted with uterus ruptured.

For the fetus the condition is extremely grave. The fetal mortality in our series was 64 per cent, 4 being dead in utero, giving a corrected mortality of 59.4 per cent. Prior to the use of adrenalin 3 craniotomies were done and 5 babies died of birth injuries, in 16 cases. Five babies were discharged alive and well. In the last 20 cases only one craniotomy has been done but 10 babies died of birth injuries. Eight babies were discharged alive and well.

Table IV consolidates the above figures.

TABLE IV

	TOTAL		PRIOR TO USE OF ADRENALIN		SINCE USE OF ADRENALIN	
	NO.	%	NO.	%	NO.	%
Maternal mortality	6	16.6	4	25	2	10
Maternal morbidity	10	27.7	3	19	7	35
Gross fetal mortality	23	63.8	11	69	12	60
Dead in utero	4		3		1	
Craniotomy	4		3		1	
Died of birth injury or intrauterine asphyxia	15		5		10	
Corrected fetal mortality	19	59.4	8	62	1	58
Babies discharged alive and well	13	36.1	5	31	8	40

SUBSEQUENT DELIVERIES

It has not been possible to follow up all these patients but seven have been delivered subsequently by the service. One patient had three subsequent cesarean sections, a second patient had a placenta previa, a third had a breech delivery and a second pregnancy with a cephalic presentation three years later. In the 7 patients who returned to our service, there were thirteen subsequent pregnancies with 8 spontaneous deliveries. Contraction ring did not develop in any of these subsequent deliveries.

COMMENT

The use of adrenalin to relax a contraction ring developing in labor has led, I believe, to decrease in the maternal mortality rate. Although the fetal mortality is still high, it is gratifying to note that fewer craniotomies were necessary on living babies, and that more babies were discharged alive and well.

surgical anesthesia, one patient, an eclamptic, being given gas oxygen anesthesia. The results are given later.

Since January, 1931, all our patients have been given adrenalin, one or more doses subcutaneously, in the treatment of contraction ring dystocia. It was found that adrenalin alone was not always sufficient to relax the ring, so that most patients were also given deep surgical anesthesia. At the present time our method of treatment of contraction ring, which has proved very satisfactory, is as follows:

TREATMENT

When a contraction ring has been diagnosed by palpation, the patient is given morphine sulphate, 0.016 gm. (gr. $\frac{1}{4}$) subcutaneously. Ether is then given to deep surgical degree, by which time the morphine sulphate has begun to have its relaxing effect also. As soon as the patient is well under ether, adrenalin 0.5 c.c. is given subcutaneously and repeated in five minutes. After ten minutes, the contraction ring is again palpated and is found relaxed sufficiently to allow extraction of the fetus by low or midforceps, or by version and extraction. In cases in which ether is contraindicated (e.g., toxemias, upper respiratory tract infections) caudal block is used. It is advisable to be in readiness to inject pituitrin (minims iii) or ergotrate (0.2 mg.) intravenously immediately after the expulsion of the placenta to control excessive hemorrhage should this occur.

METHODS OF DELIVERY

There was only one spontaneous delivery in this series as noted above. All other deliveries were effected by operative means. Table III gives the methods used.

TABLE III

	DONE	UNSUCCESSFUL
Cesarean section	1	
Breech	3	
Version and extraction	16	3
Forceps on after-coming head	6	
High forceps	6	1
Midforceps	6	2
Low forceps	3	

RESULTS

The published figures as well as our own results mark this condition as one of the gravest obstetric complications and the prognosis for both mother and child is always grave.

Michael collected 43 cases from the literature and found a maternal mortality of 28 per cent and a fetal mortality of 59 per cent. Croft reports 2 cases with 50 per cent maternal mortality and 100 per cent fetal mortality. Hopkins had three cases with no maternal mortality. Rudolph, in a review of nearly 300 collected cases, found a maternal mortality of 15 per cent and a fetal mortality of 46 per cent. His own series of 21 cases had a maternal mortality of 9.5 per cent and a fetal mortality of 28 per cent.

TRICHOMONAS VAGINALIS VAGINITIS*

INCIDENCE, DIAGNOSIS AND TREATMENT WITH SILVER PICRATE

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IT BECAME apparent following the paper of Greenhill in 1928 that many cases of *Trichomonas vaginalis* vaginitis were wrongly diagnosed or undiagnosed. Bland, Goldstein and Wenrich in 1931 showed the high incidence of this condition in pregnant women, and also that it is a factor in puerperal morbidity, so that the importance of this infestation is now well recognized.

INCIDENCE

During ten months a routine search was made for *Trichomonas vaginalis* in the vaginal canal of all white patients entering the Gynecologic and Prenatal Clinics of the Philadelphia General Hospital. For purposes of comparison the colored patients were likewise examined for a period of one month. Of the 532 patients who were examined in this series, 168 (31.6 per cent) were found to harbor the trichomonad in the vaginal canal. As may be seen in Table I there was only a slight difference in the incidence of infestation in the nonpregnant and pregnant groups. However, by comparison, the percentage of positive cases found in the colored patients was almost double that observed in the white patients. There was no seasonal variation of incidence. The patients examined were all above twelve years of age. In addition to the female patients studied, an examination of the prostatic secretion in 102 male patients was made, and in 4 cases (3.9 per cent) *Trichomonas vaginalis* was found. Although it was one of the original aims of this work to attempt to find an explanation for the mode of infection or re-infection of the vaginal canal with *Trichomonas vaginalis*, nothing conclusive was found in this series nor in the literature. Therefore, a discussion of the mode of infection will not be included.

DIAGNOSIS

The clinical picture commonly associated with trichomonas vaginitis was seen in all of the acute cases in this series. It is of interest to note that in four cases (2.4 per cent) the chief complaint of the patient was

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The authors wish to express their appreciation to Dr. J. H. Clark, Pathological Laboratory, Philadelphia General Hospital, and to Dr. D. H. Wenrich, Department of Zoology, University of Pennsylvania, for their interest and assistance in this study; and to the nursing staff of the Gynecological and Prenatal Clinics for their aid in handling the patients.

In tabulating the results no attempt has been made to differentiate contraction ring dystocia from that due to obstructed labor leading to retraction ring, because no definite diagnosis was made in the histories. However, it is important to differentiate the two conditions. Although adrenalin may relax the muscles in a retraction ring, the cause of dystocia is not removed and the case is still formidable.

In dystocia due to contraction ring, adrenalin relaxes the ring and thus removes the cause. The case may terminate by spontaneous or operative delivery, depending on the condition of the patient and the judgment and skill of the accoucheur.

Although a comparison of the results before and after the use of adrenalin does not reveal spectacular improvement, yet it is the feeling of the staff on our service that such cases are now much more easily handled than previously.

CONCLUSIONS

1. Contraction ring should be differentiated from retraction ring developing in labor because the treatment of each depends on a correct diagnosis.

2. No common factor has been noted in all cases developing contraction ring, i.e., the etiology is still obscure.

3. Adrenalin, assisted by morphine sulphate and deep surgical ether, will relax a contraction ring.

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1525 MEDICAL ARTS BUILDING

Sarkar, M. N.: Epidemic Dropsy in Pregnancy, Calcutta M. J. 29: 539, 1935.

Cases of epidemic dropsy during pregnancy are presented. This condition usually terminates the pregnancy. This unfavorable result may be attributed to a hormonal unbalance which causes vasomotor changes in the vessels of the uterus and ovary. The factor of infection is emphasized, subinvolution and damage to the heart are common.

Beri-beri and epidemic dropsy are not identical conditions. Epidemic dropsy in pregnancy may prove fatal after miscarriage. Edema of lower extremities and a brawny chocolate or coffee-like appearance and hemorrhage of the gums are typical classical signs of epidemic dropsy. Hemorrhage in the gums and in the decidua are simultaneous and are dangerous signs. Protein foods, digitalis and calcium are the routine treatment for this condition.

meter and add it to the sterile tube containing modified Ringer's solution and Loeffler's blood serum.

4. Incubate at 37.5° C. for twenty-four hours.
5. Examine microscopically for presence of the organism.
6. Subculture every forty-eight to seventy-two hours.
7. Subculture into tubes containing 0.01 gm. of gastric mucin in each test tube of modified Ringer's solution and Loeffler's blood serum.

TREATMENT

The treatment of *Trichomonas vaginalis* vaginitis as devised by DeLee in 1920 is now known as the "wet" method and has had many modifications. Originally the treatment consisted in thoroughly scrubbing the vagina with green soap and water, under anesthesia if necessary, and then a solution of 1:1,500 mercuric bichloride was applied to the vaginal mucosa. This procedure was repeated the next day and the vagina packed with sodium bicarbonate and glycerin. After this a douche of 2 per cent sodium bicarbonate was used twice daily until the symptoms disappeared. Modifications of this method of treatment met with a certain amount of success. Due to the pain caused by the treatment and the frequency of recurrences if not followed completely, this method has gradually lost favor and at present the "dry" methods of treatment of *Trichomonas vaginalis* vaginitis are in vogue.

The use of a powder was first popularized by Gellhorn who sprayed kaolin and sodium bicarbonate with 12.5 per cent acetarsone into the vagina with a special insufflator. Kaolin, quinine sulphate, and sodium bicarbonate have also been used in the "dry" treatments. More recently the use of arsenic derivatives has met with success. The dry methods of treatment are advantageous from the point of view of both the physician and the patient. In 1931 Goodall introduced 1 per cent picric acid suppositories as a treatment for trichomonas vaginitis, and in 1936 Shelanski showed that silver picrate is the most effective silver salt for destroying trichomonas in vitro. Therefore, it was decided to use as the basic part of our treatment a powder consisting of one part of silver picrate dispersed upon ninety-nine parts of kaolin.* To supplement this a suppository containing 2 gr. of silver picrate in a boroglyceride-gelatin base was used. The rationale of this method of treatment rests upon the fact that a combined antiseptic and drying agent (silver picrate-kaolin powder) is introduced into the vagina, and the time of action of the antiseptic agent is prolonged by periodic insertion of the suppositories. Our method of treatment was as follows:

After a positive diagnosis of trichomonas vaginitis had been made, the patient was placed in the lithotomy position and 5 gm. of silver picrate-kaolin powder was blown into the vagina by means of a special insufflator, care being taken to use only enough pressure to balloon out the vaginal walls. The patient was then given six vaginal suppositories of silver picrate, one to be used each night, and she was

*Supplied through courtesy of John Wyeth & Brother, Inc.

P-CARBAMINO PHENYL ARSONIC ACID IN THE TREATMENT OF TRICHOMONAS VAGINALIS VAGINITIS

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THIS report deals with the results in the treatment of *Trichomonas vaginalis* vaginitis with p-carbamino phenyl arsonic acid* (carbarsone). For the sake of brevity, this drug will be called by its trade name.

The series consists of 21 patients who came for treatment because of a vaginitis associated with annoying leucorrhea, which was foul smelling, irritating, and caused pruritus of the vulva in 17 cases. In addition, 6 of the patients complained of chafing of the thighs. In all of these patients, the motile flagellated protozoon, the *Trichomonas vaginalis*, was found in a warm, freshly made, hanging drop of a loopful of vaginal discharge taken through a warmed and nonlubricated speculum from the posterior fornix, with the addition of a drop of warm normal saline solution. If the patient had taken a douche and no trichomonads were found, she was told to omit the douching for thirty-six hours prior to her next visit for the hanging drop examination.

In addition to examining the hanging drop, gram-stained smears were studied, primarily to determine the concomitant bacteria. These two procedures were repeated each time the patient reported for examination. Before starting treatment, the stained smear usually showed (in addition to the *Trichomonas vaginalis*) many bacteria, many pus cells, a few red blood cells, degenerated cellular debris and only seldom an occasional Döderlein bacillus. As the condition improved under therapy, the pus cells became less and less until they finally disappeared, the cellular debris disappeared and was replaced by the normal epithelial cells; large numbers of the Döderlein bacillus replaced the cocci and other organisms found previously, thus showing the reestablishment of the normal vaginal bacterial flora.

In the acute and chronic stages, a gram-positive diplococcus predominated. There were also occasionally *B. coli* and diphtheroids. No monilia were found in any patient.

The age incidence was as follows: The youngest patient was fourteen years of age and the oldest forty-nine, 13 patients, or 62 per cent, being between the ages of twenty and thirty-five.

*P-carbamino phenyl arsonic acid is manufactured by Eli Lilly and Company under the trade name of Carbarsone.

The above treatment is started immediately after the cessation of a menstruation, so that it can be carried out uninterruptedly over a period of twenty-one days.

RESULTS

All patients thus treated showed absence of trichomonads and change to normal flora within two weeks. In spite of these findings, this form of treatment was continued until the end of the next menstruation to prevent a possible relapse, which is prone to recur after menstruation. The patients are instructed to return for follow-up every three months or oftener, should symptoms recur. With two exceptions, all of these patients have been found free of subjective symptoms and trichomonads after one course of treatment lasting twenty-one days.

The longest cure to date has been twenty-five months and the latest patient included in this series has been free of trichomonads for a period of three months.

The histories of the two aforementioned exceptions are as follows:

CASE 1.—Patient, aged twenty-six years, married, never pregnant, complained of marked dyspareunia and vaginitis. Trichomonads were found and treatment was instituted. All symptoms disappeared and the patient was discharged. When returning, as instructed after three months, she had her original complaints and symptoms, and on examination I again found the trichomonads and associated bacteria. I ascertained that her husband had a urethral discharge with painful urination, and that a urologist was "treating his prostate." No condom had been used. Husband denied ever having had a gonorrhea. A fresh condom specimen examined immediately after intercourse showed numerous motile trichomonads. His physician then discovered trichomonads in the prostatic secretion. We were unable to find gonococci in his secretion. Presumably, the patient had been reinfected by her husband.

CASE 2.—Patient, aged twenty-nine years, married, came for a severe leucorrhea which had been present off and on "for some time." Examination of vaginal secretion established the diagnosis of *Trichomonas vaginalis* vaginitis. Treatment was instituted and after three weeks she was pronounced free of the disease. Three months later, she was still free of symptoms, no trichomonads were found, and the vaginal flora was normal. She had no intercourse for three months since treatment was stopped. Two months later, she again reported to me because of a vaginitis, and *Trichomonas vaginalis* was found. Sexual relations had been resumed after her last visit. A fresh condom specimen revealed the presence of trichomonads; however, no trichomonads were found in the husband's prostatic secretion.

These two cases were the only failures out of 21 patients treated with carbarsone for *Trichomonas vaginalis* vaginitis; and only one deduction can be made in these two failures, namely, the husband also carried trichomonads and reinfected the wife during coitus.

Patients must be watched for toxic symptoms of carbarsone poisoning during the treatment (optic and renal changes). If a pelvic disorder exists an effort is made to correct it. Patients are impressed with the importance of active treatment also during their menstruation. At the same time they are told the proper after-care following a bowel evacuation, being careful not to spread the fecal material toward the vagina.

None of the patients who were treated were virgins. The fourteen-year-old girl had had sexual relations on several occasions. All patients were still menstruating. None of them had gonorrhea concomitant with the trichomonas infection. Parity seemed to play no rôle. Eight of the patients gave the history of having been treated by other doctors previously for the same condition.

The longest duration of discharge was in an unmarried girl nineteen years of age whose discharge started shortly after the onset of her menses and who had been under medical attention for the same complaint for a period of three and one-half years. The longest duration for the discharge without previous medical care was eighteen months. This patient was twenty-six years of age, and had to wear a protective pad constantly. She was a divorcee and denied sexual relations for the last two years. The most acute case was that of the forty-nine-year-old woman, whose symptoms were only of two weeks' duration. It was impossible to make a digital examination because of the marked vaginitis.

The treatment is carried out in the following order: Each night before retiring, the patient takes a vaginal douche with a pint of lukewarm soapsuds followed by another pint of lukewarm tap water to rinse out all of the soap. She next takes a one-half pint soapsuds enema followed by another one-half pint of plain tap water. The patient is instructed to use different nozzles for vagina and rectum and keep them separated in lysol solution. After the enema, she inserts into the rectum a suppository which contains 2 gr. of carbarsone in a glycerogelatin base which should be retained all night. After inserting the rectal suppository, she instills into the vagina by means of an Asepto one-half ounce male urethral syringe 5 gr. of carbarsone with 5 gr. of sodium bicarbonate dissolved in two teaspoonfuls of lukewarm water (carbarsone is soluble only in alkaline solution). This solution is retained in the vagina all night. On the following morning she inserts one carbarsone suppository into the vagina and another one into the rectum. In the evening she repeats the described procedure but omits the vaginal soapsuds douche, and continues in this manner for six days. Acid vaginal douches as described later are taken only as is necessary to keep comfortable. In some patients, the vaginal instillation of the carbarsone-bicarbonate solution was used in the morning and then only a suppository inserted vaginally in the evening. On the seventh day, no vaginal douche is taken, and hanging drops and smears are made. At this time, if there is subjective and objective improvement, the rectal therapy is given every night for another six nights but the morning rectal suppository is omitted. The vaginal therapy is continued for another six days. On the following day, which is the fourteenth day of treatment, the hanging drop and smears are again made. At this time she is instructed to douche vaginally every morning with a pint of lukewarm water to which is added one tablespoonful of vinegar or one teaspoonful U. S. P. lactic acid, but no carbarsone. If the douche causes burning, the same amount of vinegar or lactic acid is diluted in two pints of water. During this third week, she inserts a carbarsone suppository vaginally every night before retiring, and at the same time, a carbarsone suppository rectally every other night.

After three weeks of this treatment all rectal therapy is discontinued, and the patient takes a vaginal douche every other morning and the same evening uses a vaginal suppository, until the onset of her menstruation. During her menstruation, she douches morning and evening with the vinegar or lactic acid solution, and also uses a carbarsone suppository every night before retiring. One or two days after the cessation of menstruation, she discontinues the douches and carbarsone for at least forty-eight hours, and reports for a hanging drop and smear examination.

EVALUATION OF THE PRACTICAL USE OF THE ASCHHEIM-ZONDEK PREGNANCY TEST

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THE increasing use of the Aschheim-Zondek test for pregnancy has led us to determine, so far as possible, just what can be learned from this test. To this end, with the cooperation of the physicians involved, we have checked our results against the subsequent clinical history, when available, of those patients for whom we have made the test. A summary of the 702 cases we have been able to follow, out of over 1,100 tests, is given in Table I. In studying these data it should be kept in mind that we do not run this test routinely on all patients, but only at the request of the physician. This means that few of the average normal cases are included, and that our percentage of complicated cases, and probable errors, runs higher than in most similar studies.

It should also be noted that we have employed this test in a strictly utilitarian manner. We have used only one animal for each determination, for economic reasons, and while we have urgently advocated that only first voided morning specimens be submitted, when such were not available we have accepted others. Our percentages should not, therefore, be considered as optimal for this test. We employ immature female rats twenty-four to thirty-five days old. No preservative is used in the urine, although specimens are kept in the refrigerator. Heavy sediments, when present, are filtered off. Two cubic centimeters of urine are injected either subcutaneously or intraperitoneally each day for five successive days, and the animal is sacrificed on the sixth. With rare exceptions the results are determined by macroscopic examination. A hemorrhagic condition or corpora lutea is taken as indicative of pregnancy. Ripe, mature follicles, as such, are not considered as a positive test, but are listed as prolan A reactions.

From Table I we learn that 90.7 per cent of the tests, 327 positive and 310 negative, were confirmed by subsequent clinical findings. There were 17 false positives and 48 false negatives. Much, however, may be learned from these apparent failures. In Table II we have classified the false negatives according to their clinical histories. Of the 48, we find 17 suffered spontaneous abortion some time shortly after the test had been made. Four others gave definite prolan A reactions. Of these, one bled for nine weeks, then recovered and went to term; after the

Carbarsone has been used by a number of observers for the treatment of intestinal amebiasis. Gabaldon has used it experimentally on *Trichomonas hominis* in vitro. He found that a concentration of 0.3 per cent carbarsone was always lethal in less than seventy-two hours, and when present in sublethal concentrations the reproductive rate of the flagellates is reduced. Gospe reports using carbarsone successfully in 51 patients suffering from *Trichomonas vaginalis* vaginitis.

When given orally, there is always the danger of toxic effects. The following reports of toxic symptoms following its oral use have appeared:

Epstein has reported a death following the oral ingestion of a total of 5 gm. during a ten-day interval, given for the treatment of a nonspecific dysentery of long standing. Anderson and Reed, and Smithies report untoward effects following its use orally, with recovery of the patients upon the discontinuance of the drug. The principal toxic symptoms of carbarsone poisoning as reported were: icterus, large liver, exfoliative dermatitis, swollen ankles and wrists, photophobia, faulty vision and gastric distress. The optic findings described have been papillitis and retinal edema. Casts are found in the urine.

Although in my series of cases no toxic manifestations followed its application by rectum and vagina, I feel that patients must be watched most carefully, though I have been unable to find any report of toxic symptoms following the vaginal use of this drug.

SUMMARY

1. A report is made of 21 cases of *Trichomonas vaginalis* vaginitis treated with carbarsone.

2. In this series, there were two recurrences, which probably represent reinfections from the husband.

3. Carbarsone administered in the manner here described caused no toxic symptoms. Nevertheless, the patients should be watched closely because of the large doses of the drug used.

4. The importance of treatment also during menstruation, and the examination of the male especially in instances of seeming recurrence are stressed.

5. The treatment of the rectum is stressed because of the possibility of its being a source of infection.

6. The treatment is carried out entirely by the patient, and thus avoids all forms of office treatment, which is generally painful at this time.

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should not have been used. This may also account for some of our other 12 failures, where no complicating factors could be learned from the histories. We do not believe there is any direct relation between the specific gravity of the urine and the concentration of the hormone, but we do feel that a high specific gravity, unless from a diabetic, usually coincides with satisfactory hormone content. Unfortunately we have not recorded the specific gravities in this series, so cannot give the relation of failures to dilute urines.

In Table III we have given a similar classification of the false positives. The first was not an error of the test, since we later learned the patient had been taking antuitrin-S; after discontinuation of the drug the test became negative. We make no claim that pelvic inflammatory

TABLE III. CLASSIFICATION OF FALSE POSITIVES

	NO.	PER CENT OF TOTAL
History of taking antuitrin-S	1	5.88
Pelvic inflammatory diseases	3	17.65
Carcinoma of the liver	1	5.88
Cardiac lesions and high blood pressure	1	5.88
Menstrual disorders	6	35.30
Ovarian cyst	1	5.88
Menopause	1	5.88
Unexplained	3	17.65
Total	17	100.00

diseases cause false positives, but we did find that complicating condition in the histories of 3 out of the 17 false positives we obtained. The same is true regarding the carcinoma of the liver and the cardiac lesion case, although the latter, with a history of 8 miscarriages, might easily have suffered a ninth, unrecognized. The menstrual disorders offer grounds for doubt. In at least 3 of the 6 cases the obstetrician felt that the evidence pointed to an abortion having been performed, but lacked actual proof. Also a spontaneous abortion might easily pass unrecognized. Lacking evidence, however, we must record these as false positives. For this reason patients who, failing to menstruate, request a pregnancy test, then, after receiving a positive report, have menstruation reestablished, offer difficulties of classification.

Menopause is usually supposed to invalidate the test. We had one false positive from such a patient, but 7 others also in that condition gave correct negatives. The cyst has already been discussed, which leaves 3 false positives with no explanation. In these instances the use of only one rat may account for our difficulties. We have, however, recorded 18 cases where 2 or more animals were used in successive tests. In 15 of these cases, 2 positives, 9 negatives, and 4 false negatives, the report was unchanged. In two of the false negatives, where the patient was obviously pregnant, 3 rats each were used, all reported negative.

bleeding had been stopped the Aschheim-Zondek test became positive. A second miscarried at six months, and while the remaining two were carried to delivery, they were beyond doubt threatened with abortion when the test was made. This would indicate that these failures are

TABLE I. DISTRIBUTION OF ASCHHEIM-ZONDEK RESULTS

	NO.	PER CENT OF TOTAL
Positive	327	
Negative	310	90.75
False positive tests	17	2.42
False negative tests	48	6.83
Total run	702	100.00

TABLE II. CLASSIFICATION OF FALSE NEGATIVES

	NO.	PER CENT OF TOTAL
Spontaneous abortion	17	
Prolan A reaction (threatened abortion)	4	43.7
Early tests (under 40 days)	13*	27.1*
Dilute specimen	1	2.1
Ovarian cyst	3*	6.3*
Unexplained	12	25.0
Actual total	48	100.00

*One specimen appears in two groups.

not due to the method, but rather to some failure of the hormone itself, the presence of prolan A suggesting that the usual menstrual sequence was in progress. A negative Aschheim-Zondek report, in conflict with clinical evidence, may then be taken as evidence of a threatened abortion, and the patient treated accordingly.

In 13 of our failures the specimens were taken before the fortieth day of the pregnancy, as determined by the delivery date. The earliest positive test was obtained at three weeks. Between the twenty-first and the fortieth day we have had 25 determinations, 12 positive and 13 false negatives. We conclude from this that negative reports made on specimens collected less than six weeks from the last menstrual period are not reliable, and, unless supported by definite clinical evidence, should be repeated.

Three of the false negative cases were complicated by ovarian cysts. One of these upon removal was diagnosed as a papilliferous adenocystoma. The second disappeared, apparently as a result of the examination. The third was not removed. We also had one false positive with an ovarian cyst, and four correctly reported as not pregnant. One of these latter was a papillary adenoma. No positives were reported as having this complication. The fact that correct negative results may be found does not prove that such cysts do not complicate, and possibly invalidate, the results when the patient is actually pregnant.

The concentration of the specimen, and therefore of the hormone, is very important. One of our negative failures was very dilute, and

A MODIFICATION OF THE VISSCHER-BOWMAN PREGNANCY TEST, WITH A REPORT ON 513 OBSERVATIONS

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C DOLFF reported in 1936 that the Visscher-Bowman pregnancy test was 95 per cent correct on occasions in which it was used to diagnose normal pregnancies, and also in 82 per cent of cases of ectopic pregnancy and miscarriage.

The Visscher-Bowman pregnancy test is purely chemical, the reaction depending on the presence or absence of anterior pituitary hormones in the urine. It is performed as follows: To 1 c.c. of urine are added one drop of 1 per cent hydrogen peroxide, 5 drops of aqueous methyl cyanide solution, and 5 drops of phenylhydrazine hydrochloride solution, and 5 drops of concentrated hydrochloric acid; the mixture is heated for twenty-five minutes in a water-bath. The test is positive if a reddish brown flocculent precipitant is observed; if the color remains straw yellow and the deposit is powdery or absent, it is negative.

From the urine of 54 proved pregnant women, Dolff's series yielded a positive result in 51 cases, or 96 per cent. In 18 cases of early pregnancy the test in his hands was accurately diagnostic except for one false positive. Dolff believes that the source of error is a high concentration of catabolic reducing substance in some specimens of urine, and with these eliminated the percentage of accuracy of the test will increase.

AUTHOR'S SERIES

This series consists of 513 cases, 420 of which were sent to me by a staff member from his private practice. They were numbered, and I never saw the patients.

There were 79 specimens obtained from patients in the hospital and out-patient department. Each set of specimens was run with a control tube which contained urine of a nonpregnant female as confirmed by the Aschheim-Zondek test. In the series, 15 specimens were checked by the Aschheim-Zondek test. One specimen was from a patient with suspected teratoma of the testicle; one was from a woman who had an ovarian tumor, the nature of which was not determined as the patient refused operation; 10 specimens were from patients with incomplete abortions, and two specimens were from women with dead fetuses. Two specimens were from patients with suspected ectopic pregnancy. It was found that by using 6 drops of each of the reagents and heating the specimens in boiling water forty-five minutes a better and more easily read result was obtained. If one drop of concentrated hydrochloric acid is added to the 1 per cent solution of hydrogen peroxide when the solution is made up, it will retain its strength for a week to ten days, thus obviating the necessity of making up a fresh solution so often. This was the procedure used in each of the cases of this series.

The earliest positive test obtained was in patients who were two weeks past due in menstruating. Three such cases appear in this series. Twelve women four weeks

In the 3 cases where the second animal did give a different result, there was very definite clinical evidence of a change in the condition of the patient.

We are now investigating the hypothesis that continued negative results from a pregnant woman who goes to term and delivers a normal child, may possibly be associated with nitrogen retention. If the hormone is of a protein nature, and is secreted slowly, might it not also suffer retention from a slightly impaired kidney? This would account for negative results from even concentrated urines.

In the operation of the test certain difficulties are frequently encountered. Many types of medication interfere, usually killing the test animals. Quinine and arsenic are particularly bad in this respect. Only good healthy animals should be used. Intraperitoneal injections are tolerated better by the rat than subcutaneous. Specimens should be used fresh, although if kept cold they can be used as long as a week after collection. Foul-smelling urines usually prove fatal to the animals. With proper precautions, and employing the suggested restrictions, the success of this method may be raised considerably above the figure given in our tables.

SUMMARY AND CONCLUSIONS

Negative results from Aschheim-Zondek pregnancy tests run within the first six weeks of the pregnancy are unreliable. Positive results may be accepted.

Negative results after the first six weeks, in conflict with clinical findings, may indicate threatened abortion, particularly if the test gives a prolan A type of reaction.

Ovarian cysts complicate the situation and apparently tend to interfere with the test.

Inflammation in the region of the pelvis is frequently associated with false positive reactions.

Data obtained during menstrual disorders are difficult to classify, since unreported abortions may be recorded as false positives.

Taking into account the above-mentioned conditions, the reaction gives a very reliable test for pregnancy. As run, we had an uncorrected error of about 9 per cent.

Lévy, S.: Presentation of a Speculum Permeable to the X-Ray, *Bull. Soc. d'obst. et de gynec.* 25: 442, 1936.

The author describes a new speculum made of aluminum which can be used for hysterosalpingography. This speculum is not visible in x-ray pictures and does not interfere with shadows of the cervix and the isthmus of the uterus.

J. P. GREENHILL.

uterine pregnancy was found; therefore, they are classified as false positive reactions, due, supposedly, to increased catabolic reducing substances in the urine of these patients.

SUMMARY

Total number of tests performed	513
Total number of tests in error	40
Total number of false positive reactions obtained	20
Total number of false negative reactions obtained	20
Total number of doubtful reactions obtained	1
Total number of dead fetuses with subsequent abortions, one positive and one negative result	2
Total number of suspected ectopic pregnancies, both gave a false positive reaction	2
Total number of incomplete abortions	10
Total number giving positive reaction	8
Total number giving negative reaction	2
Total number of tests checked by the A-Z test	15
Total number of tests checked by A-Z which gave a positive reaction	8
Total number of tests checked by A-Z which gave a negative reaction	4
Total number of cases checked by A-Z which gave a false positive reaction	2
Total number of cases checked by A-Z which gave a false negative reaction	1
In 15 cases checked by the A-Z test, percentage of error	20
Correct results	80
Total number of cases of early diagnosis of pregnancy	38
Total number of patients 2 weeks pregnant with a positive result	3
Total number patients 4 weeks pregnant with positive test	12
Total number patients 5 weeks pregnant with positive test	2
Total number patients 6 to 8 weeks pregnant with positive test	17
Percentage of error for entire series	7.7
Percentage of correct results for entire series	92.3

CONCLUSIONS

1. The Visscher-Bowman pregnancy test in the total series gave 92.3 per cent correct results, and in 15 cases checked by the Aschheim-Zondek test, 80 per cent correct results.

2. It is a cheaper, easier, and quicker test than the Aschheim-Zondek and can easily be done in one's office. It is not as valuable, however, to one inexperienced in differentiating the various precipitates as C. Dolff would lead us to believe in his paper. The test requires a great deal of practice before very much accurate dependence can be placed in one's interpretation of his results. In the hands of the experienced observer it is just about as early a diagnostic test as the Aschheim-Zondek, particularly when the first voided morning specimen is used.

3. The test may be negative in cases of advanced pregnancy with a dead fetus if there is a placental separation large enough to prevent secretion of the hormone in quantities large enough to cause a positive result. This may also be the case in incomplete abortion, even though dilatation and curettage will reveal retained products of conception.

pregnant gave positive reactions. Two women who were five weeks, and 17 who were six and eight weeks pregnant gave positive results, as did, also, 4 patients who were ten weeks pregnant.

Of 15 cases checked by the Aschheim-Zondek test, there were 8 positive, 4 negative, 2 false positive reactions, and 1 false negative, an accuracy of 80 per cent. The series is very small, and no conclusions should be drawn from it.

Of the total series of 513 cases there were 40 cases in which the test was in error, or gave a false positive or negative reaction, the percentage of error being 7.7 per cent with 92.3 per cent correct results. Twenty of these 40 cases were false positive reactions, and 20 were false negative when the patients were known to be from 4.5 to 9 months pregnant. This is explained on the basis that the amount of hormone in those particular specimens of urine was not sufficient to cause a recognizable positive reaction. One case gave a doubtful reaction, and as the patient has not returned, no specimen or examination has been checked. The false positive reactions are supposed to be due to increased catabolic producing substances in the urine of these cases.

DISCUSSION

While the test is cheaper, simpler, and requires less time to perform than the Aschheim-Zondek test, it requires considerable experience in learning to differentiate the various precipitates obtained. It is often difficult to differentiate between a flocculent and powdery precipitate, especially when the quantity is very small. In such cases, it was found that the convex reflecting mirror of a microscope was of great assistance. By holding the test tube over the mirror at an angle of 45 degrees and looking into the mirror, it often became a simple matter to differentiate the precipitates. It was also discovered that by allowing the tubes to remain in a rack undisturbed for several hours the reddish brown flocculent precipitate was observed in specimens that were at first classed as doubtful.

In two women six months pregnant, whose fetuses had been dead about a week, the reactions were negative in one and positive in the other. In the case that gave the negative reaction, it was learned at delivery that there had been a premature separation of the placenta, and it was thought that the secretion of the hormone was dependent upon the intactness of the placenta to the uterine wall.

In the ten cases of incomplete abortion, it was found that 8 gave a positive reaction and 2 a negative one. It was thought that in those cases that gave a positive reaction some placental tissue was living and secreting enough hormone to precipitate this reaction. In those which gave a negative result and yet the patients presented symptoms (uterine bleeding, passage of clots, and pieces of tissue), and in whom retained products of conception were obtained by dilatation and curettage, it was believed that no placental tissue was actually living and secreting the hormone, or at least, in quantity sufficient to produce a positive result.

Of the two patients with suspected ectopic pregnancy upon whom the test was run, both were positive. At operation, however, no ectopic or

to 1929; Vienna, one to 2,000 for the last seven years and another Moscow clinic, one to 961 in a fifteen-year period from 1887 to 1902. Maljawnski⁷ finds one rupture in 1,273 cases during 1931 and 1932. In a personal communication two general hospitals in Brooklyn were found to have an incidence of one rupture to 1,075 cases⁵ and the other¹⁰ one to 1,582 during the last fifteen years.

There were 736 cesarean sections done at the Woman's Hospital, and in three, subsequent ruptures of the uterus took place, an incidence of one in 245 cases or 0.41 per cent. All of the cases here reported had a classical cesarean section.

CASE REPORTS

CASE 1.—M. S., thirty-two years old, gravida v, had an ample pelvis. In the four previous pregnancies, a placenta previa with delivery at the sixth month in the first, ten years ago; the second, eight years ago, was a premature seven months' baby, which lived; the third was a full-term normal baby; the fourth, two and one-half years ago, was induced at thirty-eight weeks because of high blood pressure, with a living baby. Five years before the present pregnancy a plastic operation and an appendicectomy were done. During the present pregnancy the patient developed a toxemia, and labor was induced ten days before time. She had indefinite labor pains for twenty-four hours. Vaginal examination disclosed a 9 cm. dilatation of the cervix through which membranes and a loop of cord protruded; presentation transverse. A marginal placenta previa could be palpated on the right side. Both feet were grasped and pulled through the cervix into the midvagina. With a contraction of the uterus, the baby, weighing 8 pounds, was born to the umbilicus and then slowly and easily extracted. The placenta was easily extracted manually. Inserting the hand into the uterus, the operator found that the cervix had split in the right posterolateral position, the tear extending through the vault of the vagina into the broad ligament and the lower uterine segment for 4 cm., a complete rupture. Uterus and vagina packed. Immediate supravaginal hysterectomy done and the patient recovered.

CASE 2.—S. S., twenty-seven years old, primigravida, ample pelvis. Myomectomy two years previously. At term, after an eight-and-one-half-hour labor, there was delivery of a six-pound-eleven-ounce baby by breech extraction; placenta by modified Credé. With only a small blood loss, the patient was returned to bed in poor condition; pulse 140, very weak; skin cold and clammy. She complained of pain in the left chest. Pulse, two hours after delivery, went to 160 and became weaker. Since her condition did not improve, laparotomy was performed eight hours after delivery. At the summit of the fundus and running from before backward, there was a rent one and three-quarter inches long. Supravaginal hysterectomy and recovery.

CASE 3.—F. B., aged thirty-one years, gravida ii, ample pelvis. Previous normal pregnancy six years ago; position R.O.P. After twenty-one hours of strong pains, there was no progress beyond engagement of the head at the pelvic brim. Therefore, version was performed and the child extracted easily as far as the head. Forceps slipped off because of hydrocephalus; basiotribe of Tarnier was used and the head was extracted easily. No shock. Baby weighed six pounds, seven ounces. Vaginal examination detected a rent in the uterus on the left side, beginning at the cervix and running up to the fundus with a ragged perforation at the base of the broad ligament admitting three fingers. Temporary packing was followed by supravaginal hysterectomy. Recovery was complicated by postoperative pneumonia.

CASE 4.—S. J., aged twenty-four years, gravida ii, ample pelvis; previous pregnancy was terminated by breech extraction of a seven-pound-six-ounce baby, four

4. There were not sufficient cases of ectopic pregnancy in this series to warrant any conclusions as to the accuracy of the test in this condition.

5. In some cases of advanced pregnancy the test will be negative. This is explained by the fact that there is more hormone in some specimens of urine than in others. Had all the specimens been morning specimens, in which it is recognized that the concentration of the various hormones is greater, some of these false negative reactions would have been eliminated.

6. While this test is not as accurate as the Aschheim-Zondek, due to the false positive and negative reactions, it is to all practical purposes a fairly accurate test for those who cannot afford the costs of the Aschheim-Zondek test, or who have not the time or facilities for doing it in order to make an early or differential diagnosis of pregnancy.

7. This is only a preliminary report.

I am greatly indebted and wish to express my appreciation to Drs. A. J. Kilpatrick and J. W. Thurmond and to their secretary, Miss Schaufele, for their assistance in furnishing specimens for this work.

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AN ANALYSIS OF 12 CASES OF SPONTANEOUS RUPTURE OF THE PREGNANT UTERUS

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THE ever increasing use of cesarean section as a method of delivery has brought to the foreground the possibility of the more frequent occurrence of one of its most serious complications in future pregnancies, namely, spontaneous rupture of the uterus.

FREQUENCY

During the period from 1914 to 1934 inclusive, there occurred twelve instances of spontaneous rupture of the pregnant uterus in the Woman's Hospital Obstetrical Service of 21,594 cases, an incidence of one in 1,800 deliveries or 0.055 per cent.

Reports in the literature vary from one rupture in 255 deliveries in a Moscow maternity² to one in 27,793 in Bombay.⁴ In 1927 Davis,³ in a thirty-six-year study of 147,625 confinements at the New York Lying-In Hospital, found one rupture in 810 cases. He quotes Williams finding one to 500, DeLee one to 2,114 and Craigin one to 1,333. McNeile and McBurney⁸ found one rupture in 578 deliveries at the Los Angeles County General Hospital in a service of 17,350 cases from Jan. 1, 1923, to March 31, 1934. Bogdanowa² reviews the findings in some European clinics: Berlin (Koblanca) one to 462; Koenigsberg (Sachs) one to 577 cases from 1919

CASE 10.—S. F., thirty-five years old, mild funnel pelvis. Her six previous pregnancies never advanced farther than the fourth month. She had been operated upon in Munich (date unknown). A myoma the size of an English walnut was removed from the right horn of a bicornuate uterus; the other horn was atrophic and removed at the same operation together with the left tube and ovary. A classical cesarean section was done at term high in the anterior wall with the delivery of a six-pound living baby. The scar where the fibroid had been removed could not be found. She was now in good health with no symptoms, two weeks postterm, not in labor, and thirteen months after her previous cesarean operation. As the abdomen for this elective cesarean section was opened, there was noted an aperture about 3 cm. in diameter through the anterior uterine wall. The membranes protruded but there was no bleeding. The opening was extended and a five-pound-five-ounce baby was delivered; although the child cried, it subsequently died. The uterine muscle was sutured, the remaining tube sterilized, and the patient recovered.

CASE 11.—C. G., aged twenty-eight years, just minor pelvis. Gravida iii, one stillborn and a classical cesarean section eighteen months previously for disproportion (nine-pound baby). Now at term. She was in labor at home for twenty-four hours. Upon admission, the cervix was one finger dilated, fetus in transverse position, no pains, pulse 108, and patient was not thought to be in labor. Four hours later, patient began to complain of tenderness over the fundus; pulse was 140. No signs of shock or collapse. At laparotomy, the placenta and clots presented in the wound and were extracted; the child, weighing 8 pounds, was dead and lying free in the abdominal cavity. The uterus showed a complete rupture along the line of the old cesarean scar. Uterine rent sewed and patient sterilized. Recovery.

CASE 12.—C. H., thirty-five years old, gravida ii. Had a previous classical cesarean section whose indication and time were unknown. Went into labor spontaneously at thirty-six weeks' gestation. After sixteen hours of ineffectual pains, a No. 1 bag was inserted into the cervix and six hours later the patient got very weak, vomited, pulse 140 and imperceptible. Laparotomy revealed a great amount of clotted blood; the uterus was ruptured wide open and the baby and placenta were free in the abdominal cavity. Fetus dead. Uterus sutured. Patient developed pneumonia, cellulitis, and phlebitis but finally recovered.

ANALYSIS OF WOMAN'S HOSPITAL CASES

The cases to be analyzed fell into three groups: (A) Noncesarean section cases, 9; (B) all cases, 12; (C) previous cesarean section cases, 3.

A. Noncesarean Section Cases (9).

TABLE I. THE LABOR

	AVERAGE	RANGE
Hours in labor	30 hours	8½ to 52 hours
Duration of second stage	2 hours and 40 minutes	1 to 10 hours
Duration of third stage	28½ min.	3 to 90 minutes

This shows that the labors were longer than average but only moderately so. The membranes were ruptured artificially in one case and accidentally or spontaneously in five. The time of rupture was difficult to determine in some cases but in four of six, rupture occurred during the first stage.

Method of Placental Delivery.—In two cases manual extraction was done; in two, a modified Credé expression; in one, normal; in one, *too early for placenta*; in two, not stated. Thus of five cases only one was delivered normally.

years previously. When four weeks overdue, patient went into labor spontaneously. Position R.O.A. After twenty-two hours of irregular labor pains, the cervix was found fully dilated, the membranes ruptured, considerable meconium and 30 cm. of pulsating prolapsed umbilical cord; head of large baby at pelvic brim not engaged. Easy internal podalic version performed on a nine-pound baby in good condition. Exploration discovered a rent in the lower uterine segment just posterior to the left broad ligament which passed through the entire musculature and peritoneum. Immediate complete hysterectomy; recovery.

CASE 5.—M. S., aged thirty-five years, primigravida, ample pelvis. Labor spontaneous at thirty-eight weeks, L.O.P. with early spontaneous rupture of membranes. After thirty-two hours of labor, the head was at the brim but not engaged; fetal heart failing. Vaginal examination showed the cervix to be fully dilated. Forceps were applied but no progress made. It was decided to do a version. When the hand was introduced now, there was a loop of cord posterior to the head, not pulsating; passing the hand alongside of the head, a rent was found in the lower segment of the uterus on the left side which extended 6 cm. up to a contraction ring partially closed around the child's neck. With great difficulty, version was accomplished. Since there was no bleeding from the tear, the uterus, lower uterine segment and cervix were packed with iodoform gauze. Condition became gradually poorer because of shock, and death occurred in thirty-six hours. No signs of hemorrhage. Cause of death not definitely known.

CASE 6.—J. R., thirty-year-old primigravida, with ample pelvis. Myoma found during prenatal care. Labor spontaneous at term with a breech presentation; membranes ruptured two hours later. After forty hours of moderate pains, it was discovered that the fetal heart was no longer heard and the cervix was not fully dilated. A No. 5 bag was introduced into the cervix. After twelve hours, this came out, and examination revealed the right foot presenting and a contraction ring in the lower uterine segment not throughout the entire circumference of the uterus but more on the left side. Difficult extraction was performed. The woman's pulse immediately became rapid. Placenta delivered manually. Examination showed a rent in the uterus three inches long, beginning on the left side of the vagina and extending into the broad ligament and up into the cervix. Hysterectomy was performed immediately. Three weeks in the hospital; recovery.

CASE 7.—E. T., primigravida. Five weeks pregnant. No history given. At operation, the peritoneal cavity was found filled with free blood and the left horn of the uterus had a tear in it 1 cm. in length. Rent was sutured. Pathologic examination demonstrated a 1.5 cm. fetus and blood clots. Recovery.

CASE 8.—L. A., twenty-eight years old, gravida ii, one miscarriage, now at term with a mildly contracted pelvis, probably of the flat variety. Went into labor spontaneously, and after twenty-six hours of strong pains at home, her physician tried to deliver her. Forceps were applied unsuccessfully. She was brought to the hospital. A persistent occiput posterior was found and delivery was performed by craniotomy on a nine-pound baby. An incomplete rupture of the uterus being found (site not stated), hysterectomy was performed. Recovery.

CASE 9.—M. R., thirty years of age. One child three years previously by difficult forceps delivery; now four and one-half months pregnant. During present pregnancy, had had almost daily moderate vaginal bleeding with no pain. On the morning of admission, the patient bled painlessly and profusely and her doctor gave her chloroform and "operated upon her." Upon admission, the cervix was found to be lacerated and an incomplete tear in the lower uterine segment on the right side involving the broad ligament was found. Anterior colpotomy and suture were performed. Recovery.

The pelvis was ample in 66.6 per cent of the cases: where contraction was present, it was of the justominor or mild funnel type. In only one case was there a toxemia of pregnancy.

TABLE VI. PREVIOUS OPERATIVE OBSTETRIC DELIVERIES, ALL CASES (12)

	NO.
Cesarean section	3
Breech extraction	1
Placenta previa with induction	1
Forceps	1
None (5 are primigravidas)	6

Of the 12 cases of rupture, 9 were within two weeks of term. Among the other 3, one was four weeks past term and the other 2 were early gestation.

C. Previous Cesarean Section Cases.

The three previous cesarean section patients all had the classical type of operation; one eleven years previously for a bicornuate malformed uterus, another two years previously for disproportion and in the third there was no information on these points. The duration of labor in our three cases was twenty-eight hours, twenty-six hours, and none. No case was induced and one patient was not in labor. In two patients, the rupture was discovered at operation; all three patients were delivered by laparotomy. Abnormal presentations or complications thereof might have been a factor in rupture because one patient had a transverse position and the other had the baby presenting by the vertex, but there was edema of the meninges present. It is interesting to note that in the two patients who went into labor, cervical dilatation was poor because of weak pains.

TABLE VII. PROBABLE CAUSE OF UTERINE RUPTURES

I. Intrinsic:	
A. Changes in uterine muscle cells	2
B. Fibrosis postcesarean section	3
C. Congenital abnormalities	1
II. Extrinsic:	
Associated with manual or instrumental manipulation during the labor	6

TABLE VIII. RUPTURE IN NONCESAREAN SECTION CASES (9)

Type:	
Complete	6
Incomplete	3
Site:	
Left side	5
Right side	2
Anterior wall	0
Summit of fundus	1
Unknown	1
Cervix:	
Involved	5
Not involved	2
Not stated	2
Time from delivery to diagnosis:	
Immediate	4
Delayed	2
Not stated	3
When rupture occurred	All during second stage

Patients not previously subjected to cesarean section had complete ruptures twice as often as incomplete ruptures.

Version and breech extraction were the usual mode of delivery preceding rupture of the uterus.

Where condition of the cervix before delivery was known it was found that in two of seven cases, or 18.6 per cent, this only partially dilated.

TABLE II. METHOD OF DELIVERY (9 NONCESAREAN SECTION CASES)

	NO.
Version and breech extraction	6
Craniotomy	1
Five weeks' gestation	1
Not stated	1

TABLE III. PRESENTATION AND POSITION IN NONCESAREAN SECTION CASES

	NO.
Transverse	1
Breech	2
Occiput posterior	3
Too early pregnancy	1
Not stated	1

TABLE IV. COMPLICATIONS

	NO.
Placenta previa	1
Prolapsed cord	3
Bandl's ring	2
Antepartum bleeding	1
Persistent occiput posterior	3
Hydrocephalus or edema of meninges	2
Dry uterus from early rupture of membranes	2
Myoma	1

B. All Cases (12).

There were only two of eleven cases without some complication of presentation.

The ages of patients ranged from twenty-four years in the youngest to thirty-five years in the eldest, with an average of thirty years of age.

The weights of the babies varied from 3¼ pounds (1,470 gm.) in the smallest to 9 pounds (4,080 gm.) in the largest with an average of 7 pounds (3,180 gm.). Big babies were not a factor in this series.

TABLE V. PREVIOUS OPERATIONS—ALL CASES (12)

	NO.
None	5
Cesarean sections	3
Plastic and appendicectomy	1
Myomectomy	2
Appendicectomy	1
Amputation of atrophic horn of uterus	1

There were 41.7 per cent of the patients who had no previous operative procedure. If previous cesarean sections are excluded, four of nine patients, or 44.4 per cent, were operated upon previously.

Rupture of the uterus occurred five times in patients pregnant for the first time and seven times in multiparas (58.3 per cent).

Six of seven patients previously pregnant had operative deliveries. One-half of these were cesarean sections.

A HISTOPATHOLOGIC STUDY OF A CASE OF INTRA-FOLLICULAR OVARIAN PREGNANCY*

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THE occurrence of a case of primary ovarian pregnancy is sufficiently rare to warrant recording, although the number of case reports in the literature is steadily increasing.

Mrs. E. A., colored housewife, twenty-four years of age, was admitted to the hospital, March 16, 1916. Her chief complaint was "excessive menstruation."

She was married five years, husband living and well. She has two children in good health, three years and sixteen months of age, respectively. Her last confinement was Oct. 24, 1915, and was normal. She nursed her last child up until the time she entered the hospital. No miscarriages.

Menstrual History.—Menstruation began at fourteen years of age, occurred every twenty-eight days, and the flow lasted from five to seven days. Menstruation was always painful on the first day.

Present Illness.—Patient states that on Feb. 18, 1916, she had cramplike pains and began to flow. About two days later she passed a "fleshlike" mass, and the flow was rather excessive. This continued for a period of two weeks, during which time she passed many large clots. She took some medicine from her family physician and the flow stopped for five days, after which time it started again, although the clots were smaller, and she then decided to enter the hospital. At the time of her admission the flow was painless, but she felt very weak.

Physical Examination.—On March 15, the day of her admission, showed a small woman with pale mucous membranes, who was obviously very weak. Temperature 98.6°, pulse 90, and respirations 20. Heart and lungs were normal. Blood pressure 110/80. Red blood cell count was 3,400,000. Hemoglobin 65 per cent (Sahli). White cell count 8,200. On bimanual examination, a freely movable, painless mass was felt in the region of the left ovary. It was about the size of a lemon. The diagnosis of left ovarian cyst was made.

Operation.—Laparotomy operation was performed on March 28, 1916, by Dr. W. A. Warfield, and what seemed to be an ovarian cyst and part of the fallopian tube was removed. Upon section of the mass after operation, a fetus within a sac in the ovary was found. Her operative convalescence was uneventful.

Macroscopic Pathologic Examination.—The specimen consisted of an enlarged left ovary, fallopian tube, and mesosalpinx.

Left fallopian tube was 6.7 cm. in length. It measured through the ampulla 7.5 mm., which was its greatest diameter, while through the sectioned uterine end it measured 4 mm., which was its smallest diameter. All the fimbriae were free and appeared normal. The fimbria ovarica was well defined, free from adhesions, and connected the fimbriated extremity of the tube to the ovary. The ostium abdominale was patent. The tube was of a yellowish gray color, excepting at a point about 2.5 cm. from its uterine end, over which area the tube was dark red in color (due

*For lack of space it is not possible to include all of the authors' confirmatory illustrations.

MORTALITY—FETAL AND MATERNAL

A. Fetal.—Of the twelve cases, there are ten to consider because in one there was a five weeks' embryo and in another, the status of the fetus is not given. Three living children were obtained and seven stillborn. However, in previous cesarean section cases, all three children died, a mortality of 100 per cent; in noncesarean section cases, the mortality was four in seven. Reports in the literature vary: Lobenstine⁶ 70 per cent; Michailoff² 93 per cent; Davis³ finds an 80 per cent fetal mortality in previous cesarean section cases and those without a previous cesarean section alike; McNeile and McBurney⁸ find 60 per cent in cesarean section cases and 65 per cent in noncesarean section cases.

B. Maternal.—One death, in twelve cases, or a mortality of 8.5 per cent, occurred. It is worthy to note that this case was an incomplete rupture of the uterus which was not operated upon but treated by intrauterine packing. Sandler⁹ quotes Weber as finding 70.8 per cent mortality in 1910 and Kupferberg 66 per cent in 1927; Davis³ has a general mortality of 60 deaths in 106 cases or 56.6 per cent, but previous cesarean section cases alone have a mortality of only 12.5 per cent; Sachs² 60 per cent; Snequireff² 48 per cent; Sakharoff² 50 per cent; McNeile and McBurney⁸ 20 per cent mortality in previous cesarean section cases and 90 per cent in cases not subjected to previous cesarean section.

SYMPTOMS AND DIAGNOSIS

These cases show that rupture of the uterus can occur without dramatic phenomena commonly described. In 3 cases, the severity of the symptoms were not described in detail; therefore, only 9 are to be considered. Of these, 5 had no symptoms whatsoever and diagnosis was made by vaginal examination following the operative delivery in 4 and when cesarean section was being performed on the other, a previously sectioned case. Four patients had symptoms; 2 were operative deliveries showing postpartum signs of shock, pain in the left chest, weak pulse; 2 previously sectioned patients had no signs of shock but demonstrated only increased pulse rate, growing weaker, and pain in the abdomen. Thus, shock is to be expected in only 33.3 per cent of rupture cases and not at all in patients having a previous cesarean section.

SUMMARY

The causes of uterine rupture fall into two groups:

a. *Extrinsic overdistention type:* which is accompanied by some obstetric maneuver such as version and extraction, craniotomy, or forceps.

b. *Intrinsic type:* which includes congenital abnormalities of the uterus, fibrosis, postsection and various changes in uterine muscle cells from numerous causes.

Conservative obstetrics and repeated section if labor does not terminate quickly and successfully will prevent most ruptures of the uterus. This prophylaxis is the best form of treatment. Hysterectomy is the operation of choice for uterine rupture above the cervix; previous cesarean section cases that tear should be re-sutured and sterilized if necessary.

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Microscopic Pathologic Examination.—The specimen was preserved in Craig's solution. The pieces of tissue removed for microscopic study were washed in running water for two days, so as to rid them of all traces of Craig's solution. They were embedded in paraffin, stained with hematoxylin and eosin, and mounted in Canada balsam. Sections were made through the uterine end of the tube, the middle of the tube, just inside of the fimbriated extremity of the tube, and through

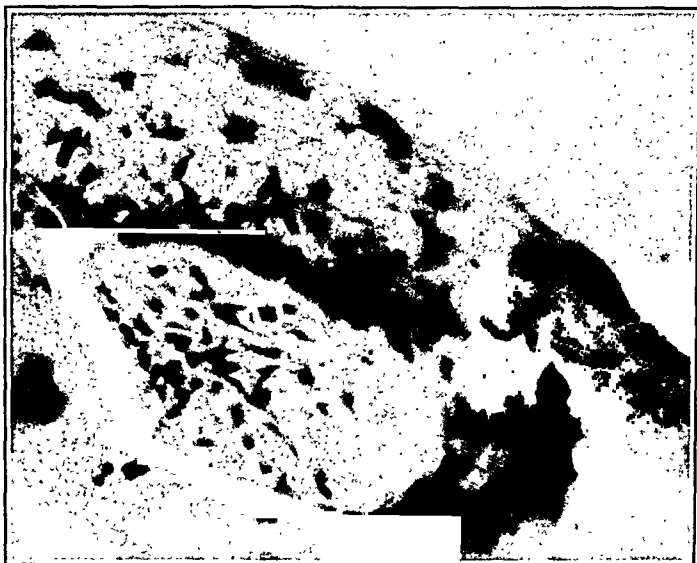


Fig. 1.—Oil immersion view of a villus in direct contact with ovarian tissue

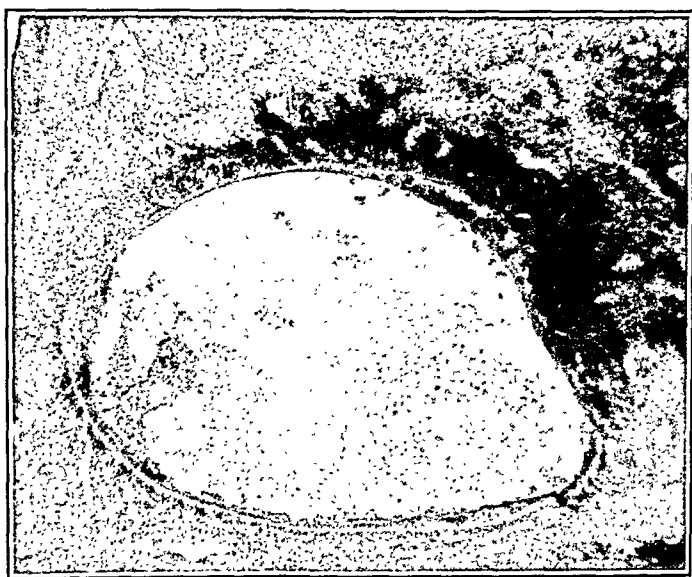


Fig. 2.—Low power. Ovarian stroma with graafian follicle, which contains a partial cumulus oophorus. This section is from the thickest part of the sac wall.

the fimbriated extremity. One section was taken from the mesosalpinx subjacent to the fimbriated extremity. Sections were taken from 10 different places in the sac wall, each equidistant from the other. One section was taken from the sac wall at the point where the cord became continuous with the amnion, i.e., site of placentation.

Left fallopian tube: The mucosa in all sections was normal. The muscular layers were well defined and normal. There were no decidual cells, nor was there any

to clamping at the time of operation). The tube was tortuous but apparently normal, except for the dark red area mentioned above. There were no adhesions, kinks, or any evidence of rupture.

Mcsoalpinx contained in its outer part a rather well marked oöphoron, and appeared normal.

Left ovary was a somewhat irregular oval mass measuring 6 by 4.5 by 3.6 cm. Several low roundish elevations, varying in diameter from 1.5 to 3 cm., form part of its outer surface, while the remainder of this surface presented numerous smaller roundish elevations, that varied from 2 mm. to 1 cm. in diameter. Some of these smaller dome-shaped swellings occurred upon the tops and sides of the larger elevations. These smaller elevations were cystic, and most of them were yellow in color, although a few were the color of chocolate. The yellowish colored ones yielded when opened a thin yellowish fluid, while the dark colored ones contained a coagulum of old blood. A smooth and somewhat glistening membrane covered the surface of these cysts as well as the intervening depressions. This membrane (tunica albuginea) presented no adhesions, but beneath it several small and very tortuous blood vessels coursed for short distances at different places. One relatively large vessel was seen which became evident about the middle of the inferior aspect of the ovary and ascended vertically on the posterior surface, then divided into three smaller branches, each of which after a very tortuous course disappeared within the ovary at or near the base of one of the cystic swellings. The ovarian ligament was about 5 mm. in length from its sectioned end to its ovarian attachment. It appeared normal.

On vertical section there was seen, situated near the center of the ovary, an oval cavity which measured 2.1 by 2.2 cm. in its vertical and transverse diameters, respectively. Its greatest anteroposterior diameter was 1.9 cm. The cavity contained a small embryo and was filled with liquor amnii. The embryo was attached to the cavity wall by a short cord. The cavity was lined with a glistening amniotic membrane. The tissue surrounding this cavity was reddish brown in color, and fairly firm in consistency. Near the external surface of the ovarian mass were a few small cavities, resulting from incisions of some of the small cysts, seen on the external surface of the mass. The cavity was located at a distance of 6 mm. from the inferior surface of the ovary: that is, the thinnest portion of the sac wall, at which point was the attachment of the placental anlage (where the cord joined with the amnion). A distance of 1.9 cm. separated the cavity from the superior surface of the mass: this represented the greatest distance of the cavity from the external surface, or the thickest portion of the sac wall.

The embryo measured, from the extreme tip of its cephalic end to the tip of its caudal end, 15.5 mm.; this was with its body bent. It measured from the small projection, which occurred just below the head to its caudal extremity, 12.5 mm. Its body was somewhat flattened transversely, which increased the anteroposterior diameter, and diminished the transverse diameter. The anteroposterior diameter, just above the umbilical region was 7 mm., while the transverse diameter was 4 mm. throughout. Four small limb buds, indicating the site of future extremities, were present. The optic vesicles were seen as two very dark circular spots on each side of its head. Its sex could not be differentiated. A part of the amnion covered the upper part of the body of the embryo. The cord presented one twist; it measured 7.5 mm. in length and 15.0 mm. in diameter. When the specimen was immersed in water, the cord kept the embryo, which floated, attached to the sac wall. There was no macroscopic evidence of a placenta. The cord joined with and apparently became continuous with the glistening amniotic membrane lining the wall of the cavity.

some were empty. The muscular coats of the arteries were very thin in places and showed many hyaline changes in the media. Small areas of extravasated red blood cells were present here and there in the ovarian stroma. Two sections from the cortex from different portions of the sac wall exhibited graafian follicles. Three were present in one section, and appeared normal. One of the follicles was 3 mm. in diameter. Two follicles showed the membrana granulosa with an external and internal tunica, and portions of a cumulus oophorus. One follicle showed an undeveloped ovum. In another section a relatively large follicle was flattened out by pressure and in it one could make out only the membrana granulosa and the tunica internus and externus. Several primordial follicles were seen in this section. Two sections from different portions of the sac wall showed corpora albicantia—one was of relatively large size; these sections contained no follicles. In the section that showed villi within the ovarian stroma, there were noted groups of polygonal cuboidal cells with round, central, deeply staining nuclei, that had a pale cytoplasm. It was easily apparent that they were not stroma cells, and on close scrutiny it was seen that they were derived from the Langerhans cells of the villi; and in places the connection between these cells and the villi could be made out. In the stroma areas nearest the blood clot and especially near the hilus were groups of altered lutein cells; they had lost their yellow pigment. The cells were relatively large, polyhedral or octohedral in shape, with a cytoplasm that did not stain. The nucleus was central, and contained a definite nucleolus. In other portions of the stroma, which showed the greatest pressure changes, these cells occurred often in single rows surrounded by stroma, and their characteristic morphology was not so evident. At the edge of the blood clot, they frequently occurred singly surrounded by hyalinized connective tissue. Many showed degenerative changes; vacuolation was the most frequent alteration. A few of the cells showed yellow pigment, which, however, was not the characteristic pigment of lutein cells. The preserving fluid probably dissolved out the pigment from these cells. Hyaline degenerative changes of the stroma was present in many places. In certain places there was marked proliferation of the stroma connective tissue along the edges of the blood clot; the young fibroblasts extended into the clot in many places, representing an attempt and organization. Foci of necrosis and leucocytic infiltration were also scattered throughout the stroma; the leucocytes undoubtedly acting as phagocytes. In one section numerous eosinophiles were present in the stroma. The layer of germinal epithelium on the external surface was represented by groups of cuboidal cells here and there on the free surface of the ovarian cortex, among which no germ cells were distinguishable. There was no evidence of a tunica internus or externus surrounding the gestation sac. The site of placentation showed only villi and intervillous spaces filled with blood. There were no decidual cells seen in any of the sections. There was nothing in this case to suggest endometriosis as a causative factor.

Ch'en, K. C.: A Case of Pregnancy at Term Complicated by Complete Atresia of the Vagina, Chinese M. J. 50: 917, 1936.

The patient in the third month of pregnancy went to a woman in her native town, who gave her a medicated tampon for vaginal application in the hope of inducing an abortion. The tampon contained some caustic material, probably a crude potash preparation. The application resulted in complete atresia of the vagina necessitating a cesarean section, followed by total hysterectomy. Recovery was uneventful.

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evidence of inflammation. Outside the muscular layer in two sections, there was some extravasation of blood between the two layers of the broad ligament (due to trauma at operation). The fimbriae were normal.

Mesosalpinx was represented by a number of blood vessels and a few epithelial-lined tubules surrounded by connective tissue. Many of the arteries were well developed, as shown by their marked muscular walls. No inflammatory reaction or hemorrhage was noted.

Sections from the sac wall showed internally fetal membranes, externally ovarian stroma, separated by a blood clot which comprised the greater part of each section.

The fetal membranes were composed of a normal amnion that was intact, in which the clear cuboidal epithelial cells were characteristic. The amniotic mesenchymal layer blended in many places with the chorionic mesenchymal layer; elsewhere it was connected by a few delicate strands of connective tissue. The cells constituting the amniotic and chorionic connective tissue were for the most part spindle-shaped, although in places some were stellate. Adjoining the chorionic mesenchymal layer was a well-marked trophoblast; the cells comprising it had round small or oval nuclei rich in chromatin. The cytoplasm was clear. These cells occurred in groups, a few singly, separated by blood spaces. A small amount of canalized fibrin was present associated with these cells. The cells were polygonal and sent out rayed processes.

The layer of blood clot: This layer made up most of the wall of the gestation sac; beginning with the trophoblast internally, it extended to the limiting ovarian stroma externally. Concentric lamellation was present. Each section showed numerous chorionic villi, completely surrounded by red blood cells in the intervillous spaces. Many villi were normal; others showed degenerative changes. The external syncytial layer with an internal layer of cuboidal Langerhans cells was distinctly seen in many of the villi; some showed only the Langerhans cell layer, while in others only the syncytium could be made out. Myxomatous tissue completely filled some of the villi; other villi showed one or more thin-walled small blood vessels containing erythrocytes. The Langerhans cells were clumped in places, forming several rows of nuclei. The syncytium sent out pointed processes here and there into the blood clot. In a few places villi were seen beginning as out-shoots from the trophoblast. In one section one or two villi were seen in direct contact with the ovarian stroma, without any interposition of blood or fibrin. The degenerating villi did not take the stain well, and the cell outline was lost. The nuclei were entirely absent in many places, while in others the nuclear chromatin was represented by numerous small granules scattered throughout the cytoplasm, which stained deeply with hematoxylin. Hyaline degeneration was present in some. Some of these necrotic villi were completely surrounded by polymorphonuclear leucocytes, which also had replaced the myxomatous core of these villi. All stages of cell destruction to absolute cell disintegration and disappearance were present. A well-defined fibrin layer was present in the outer zone of the blood clot, which lay between the villi and the ovarian stroma except in one section where the villi were lying in the ovarian stroma.

Foci of necrosis and leucocytic infiltration interrupted the continuity of the fibrin layer in a few places.

Ovarian stroma: This formed the external boundary of the blood clot. It was thickest near the hilum and became very thin below. It was thinnest opposite the point where the cord became continuous with the amnion, at which site it was represented by a layer of cells about a dozen rows in thickness. These cells were flattened out as a result of pressure exerted by the clot and contained very few blood vessels. The stroma was intact throughout, and showed no point of rupture. The stroma near the hilus was most abundant and showed little or no pressure changes. Here it was very vascular; many of the blood vessels contained red blood cells;

Blood for autotransfusion has been obtained by various methods, treated in many different ways and administered to the recipients by a variety of technics. In gynecology and general surgery, the blood escaping from tubal pregnancies or from ruptured viscera has been allowed to remain in the peritoneal cavity for absorption. At other times it has been removed from the peritoneal cavity by a suction apparatus or a syringe or has even been dipped up by cups or squeezed out of tampons and then returned to the patients' veins. In general medicine, especially in blood disorders, it has been procured from the patients' veins, treated by radium, x-ray, chemicals, or kept in an incubator before being returned to the circulation. In obstetrics, blood obtained from the placenta has been given by rectum. Farrar¹⁶ in her article, describes a technic similar to the one employed by me. She used this form of transfusion in patients where blood had escaped into the peritoneal cavity during hysterectomy and from tubal gestation.

Sampson¹⁷ in two articles published several years ago showed, by the injection of the blood vessels of myomatous uteri, that there is a great increase in the blood supply of uteri containing these tumors and that the subserosal veins of the uterus and tumors are greatly enlarged. MacFee¹⁸ states: "It is a matter of common observation that fibromyomata of the uterus, whether pedunculated or sessile, frequently present large, tortuous, thin walled, subserous veins. It occasionally happens that one of these large vessels becomes ruptured producing serious intraperitoneal hemorrhage." These engorged veins are readily accessible for recovering the blood present in the large myomatous uteri.

In order to learn how much blood may be removed with uteri which contain myomas and also with uteri which are free of gross pathologic changes, the following data were collected by me and are presented in the accompanying tabulations. During panhysterectomy the blood supply of the organ was cut between clamps or sutures so that whatever blood the organ contained was removed with it. As soon as the specimen was removed, it was placed in a basin, the clamps or sutures were removed and the blood was allowed to escape from the uterus. Forty uteri were studied in this manner. Twenty-five of these uteri were grossly normal and had been removed for various reasons. The remaining fifteen uteri contained myomas of various sizes. The normal-appearing

TABLE I. THE WEIGHT AND AMOUNT OF BLOOD IN MYOMATOUS UTERI

HOSP. NO.	AGE OF PATIENT	WT. OF UTERUS IN GM.	AMOUNT OF BLOOD DRAINED C.C.
6881	47	2830	270
12380	48	4100	425
6788	46	2100	20
453	44	2730	220
1185	28	840	24
25442	45	2690	240
422-35	55	1810	250
4749	47	3960	410
10840	38	2230	210
2786	46	1360	100
1907-35	42	1580	200
5403	47	1360	160
10140	36	1910	270
276-35	42	2880	380
8599-33	46	9971	950

AUTOTRANSFUSION WITH BLOOD FROM LARGE MYOMATOUS UTERI

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TRANSFUSIONS are often employed for the satisfactory recovery of patients who have had myomatous uteri removed. In this paper I am presenting a practical method for autotransfusion in which the blood in the myomatous uteri is recovered and returned to the patient. This procedure, used successfully in two cases, has been prompted by the following observations: first, a large amount of blood almost invariably escapes from the specimen after it has been removed and placed in a basin, and second, the presence of frequently engorged subserosal veins of uteri containing large myomas.

The advantages of this method are that there is no necessity of another donor and the blood is immediately available when urgently needed.

Cottis,¹ in his discussion of the value of auto blood transfusion, states: "In the event of severe hemorrhage into the abdominal cavity, whether it is before or during operation, it is not good surgery to throw away the blood. This method of returning it to the patient is simple, safe, and effective. It is a conservative measure which is worthy of more general use."

Moreover there is no fear of the foreign protein reaction which may follow in so-called true blood matching.

Levine and Segall² in their studies on posttransfusion reactions state: "A long operation in which ether is used alters the patients' serum as regards its hemoagglutinin properties. This is not permanent but disappears in the first twenty-four hours after operation."

Autotransfusion, autohemofusion, and autoinfusion are used synonymously in the literature. Autotransfusion was employed successfully in 1914 by Johannes Thies³ of Leipzig. He reported three cases of ruptured ectopic pregnancy where he procured the blood free in the peritoneal cavity and returned it intravenously to the patient. Previous to this time the English mentioned the advisability of autotransfusion and used it in several cases of leg amputations. Lichtenstein⁴ in 1918 reported its use in 39 cases of extrauterine pregnancy. The first article on this subject to appear in this country was published by White⁵ in 1923. Autotransfusions in ruptured tubal pregnancies have been reported by May,⁶ Cottis,¹ Maynard and Rees,⁷ Appleby,⁸ Love,⁹ and Ricci and Di Palma,¹⁰ and others. In 1923 Burch¹¹ summarized 164 cases, all European, with only two deaths. Davis and Cushing¹² described a method for autotransfusion, using the blood lost during prolonged neurosurgical operations. Gray¹³ obtained the blood after splenectomy and used it with good results. Coley¹⁴ reported a case of autotransfusion where the blood from a traumatic ruptured spleen was employed. Recently Watson and Watson¹⁵ reported the successful use of autotransfusion in the treatment of a patient who had a laceration of the heart.

tached is extended to the specimen. The suction flask and tubes are all sterilized before operation. The instrument nurse washes out the flask and tubing with normal saline and then places 40 c.c. of 2 per cent sodium citrate solution in the flask. It is now ready for use. In the cases reported, a No. 12 gauge needle was inserted in the large subserosal veins of the uterus and those of the mesosalpinx. These veins were very large in both cases. Continuous suction could not be employed because the wall of the vein would collapse against the opening in the needle. This difficulty was overcome by compressing the tube and shutting off the suction and allowing the veins to be filled by gravity or massage. In the first case 500 c.c. of blood was obtained from the uterus and in the second case 380 c.c. of blood.

The operator can proceed without difficulty while the suction is working. Now and then the instrument nurse rotates the flask containing the blood, citrate, and saline solutions. After sufficient or all the blood is obtained, the instrument nurse filters the blood through at least twenty thicknesses of gauze and measures it. If more of the 2 per cent citrate is needed to make the citrate solution 10 per cent of the total volume, the necessary amount is added. While the blood is being prepared, an interne starts an intravenous injection of normal saline, so that he is ready to give the citrated blood as soon as it is filtered. The blood is kept at body temperature by immersing the flask in warm water. In the two cases reported by me, the transfusion was completed before the abdominal operation was finished. On account of the possibility of malignancy being present in a myomatous uterus, either in the form of sarcoma or an associated adenocarcinoma of the uterine mucosa, even in women before the menopause, it would be wiser to collect the blood, but not use it until after the uterus has been removed and incised. If necessary, frozen sections can be made and examined.

Although the cubital vein has usually been used, any vein, even a large vein of the omentum, can be used if the brachial vessels are collapsed and the abdominal cavity is exposed.

Citrated blood has been used without danger. When one considers that if 1,000 c.c. of citrated blood are given, the patient receives only 2 gm. of sodium citrate. This method may be considered feasible since over twice that amount of sodium citrate may be safely given to the patient.

CONTRAINDICATION TO THE USE OF AUTOTRANSFUSION IN GYNECOLOGIC OPERATIONS

The contraindications to autotransfusion are three: infection, malignancy.

A careful examination of the peritoneal cavity for evidence of infection should be made at the time of operation. If any such evidence is found, the blood should not be used. It is also possible that bacteria may be introduced into the blood stream of the patient as a result of faulty technic.

The greatest contraindication to this procedure in myomatous uteri is the possible presence of sarcomatous changes in the myoma or an associated carcinoma of the uterine mucosa. A large percentage of women between thirty and forty years of age have uterine myomas. Some of these will have malignant changes of the uterus in later years. Since uncomplicated myomas usually decrease in size after the menopause, any increase in size of a myomatous uterus after that time should be looked upon as an indication of possible sarcomatous change in the myoma.

uteri weighed from 95 gm. to 152 gm. and yielded not more than 5 c.c. of blood. The fifteen uteri containing myomas weighed from 840 gm. to 9,971 gm. and drained from 20 c.c. to 950 c.c. of blood.

Obviously there is a fairly constant amount of blood drained from a normal-sized uterus, while the blood obtained from myomatous uteri using similar methods is greater. Moreover, the amount of blood obtained from a myomatous uterus is not directly proportional to the size of the tumor. Even fairly large myomatous uteri may sometimes contain very little blood, as shown in Table I.

TECHNIC

In the two cases reported in this paper blood was obtained from myomatous uteri before removal but after their blood supplies had been ligated or clamped and

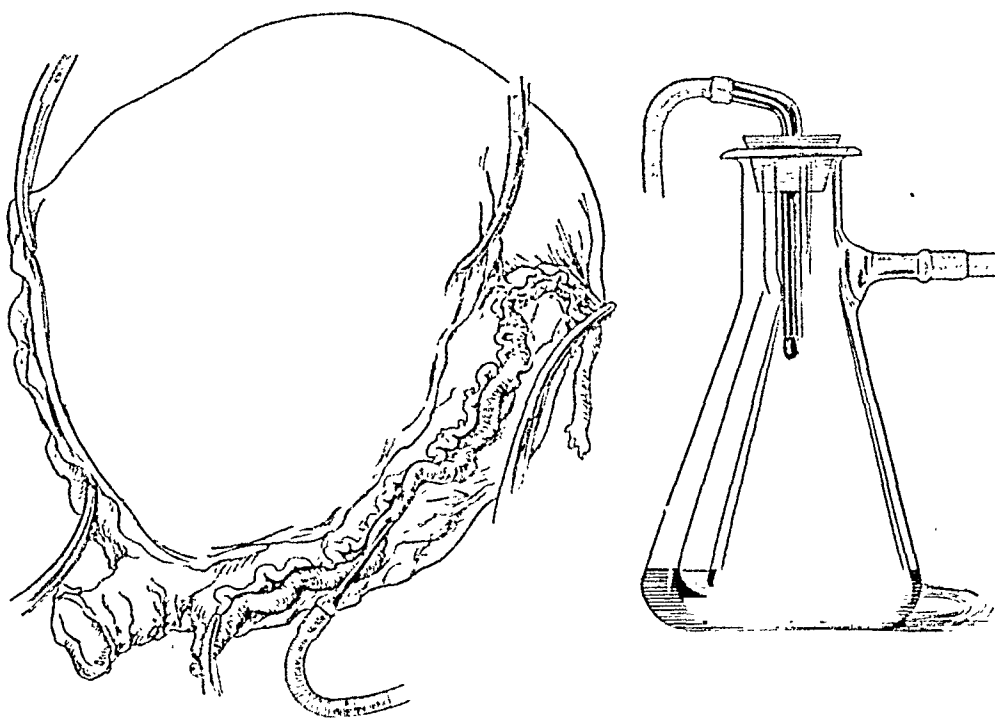


Fig. 1.—A large myomatous uterus after its removal is shown. A needle is inserted in a large uterine vein between the layers of the broad ligament. The flask at the right is situated on the instrument table. The tube inserted in the rubber stopper of the flask is a continuation of the tube with the needle inserted in the vein. The tube from the side limb of the flask is continuous with the bottle on the floor near the radiator. Another tube extends from this same bottle to the radiator which is the source of suction.

then immediately returned to the patients' circulation by intravenous transfusion. The apparatus used for recovering the blood from these myomatous uteri is a suction outfit similar to the one ordinarily employed in recovering fluids in the course of abdominal operations. This consists of a source of suction which, in the operating room of the Albany Hospital, is the radiator. A large bottle with a two-holed rubber stopper is placed on the floor near the radiator. Through one opening in the stopper a glass tube with a rubber delivery tube is attached to the source of suction. Through the other opening a tube is connected with a suction flask on the instrument table as shown in Fig. 1. The suction flask on the instrument table is plugged with a one-holed rubber cork. From a side limb in the flask a tube is attached to the source of suction. Through the hole in the rubber stopper a tube with needle at-

used because of the fear of contamination from the cervix. The uterus, after the removal of the blood, weighed 9,971 gm. The patient was discharged in good condition on Dec. 23, 1933.

CASE 2.—Mrs. H. K., aged forty-two years (No. 276-35), and the mother of one child, was admitted to the Albany Hospital, Jan. 8, 1935, complaining of profuse, vaginal bleeding of four weeks' duration, increasing weakness, and shortness of breath. Her menstrual periods began at the age of fourteen, recurred at intervals of twenty-eight days and lasted for about five days. However, in the past few months, the flow had been increasing in amount and duration. The only other significant fact in her history was a loss of twenty pounds in the past six months. This, she explained, was due to a self-regulated rigid diet.

The patient was well developed and well nourished. Her heart and lungs were normal. The abdomen was moderately distended by a hard, firm tumor mass which extended from the symphysis to about two fingerbreadths above the umbilicus. Hemoglobin was 54 per cent and red blood count 3,400,000.

Under ether anesthesia, a large multinodular myomatous uterus and the left tube and ovary and appendix were removed by Dr. Sampson. After its blood supply was ligated, 380 c.c. of blood were obtained from the uterus. This blood was properly citrated, filtered and returned to the patient's circulation. The patient made a normal convalescence and was discharged Jan. 27, 1935, in good condition. The uterus, after the removal of the blood, weighed 2,690 gm.

SUMMARY

1. Autotransfusion is a standard procedure in the Gynecological Service of the Albany Hospital.

2. In selected cases blood may be obtained from a myomatous uterus during the operation or after the uterus is removed and returned to the patient intravenously as soon as the operator is sure that malignancy is not present in the uterus.

3. A simple technic for this purpose is described.

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Approximately 80 per cent of the patients with cancer of the body of the uterus are past the menopause. This coincides with the percentages obtained from my study¹⁹ of the cases of carcinoma of the body of the uterus occurring in the Gynecological Service of the Albany Hospital from 1921 to 1931. A large percentage of the patients with cancer of the body of the uterus also have uterine myomas. In view of the above clinical data, any woman at or after the menopause who complains of uterine bleeding, even if myomas are present, should have either a panhysterectomy or a diagnostic curettage if for any reason the former is contraindicated. In the latter instance, the blood of the specimen should not be used for transfusion purposes if malignant changes are present in either the endometrium or myometrium. If there is any suspicion of the possibility of either form of malignancy being present in a case the blood may be obtained and kept until a microscopic report of a frozen section is secured.

REPORT OF CASES

CASE 1.—Mrs. R. J., aged forty-six years (No. S599-33), married and the mother of three children, was admitted to the Albany Hospital, Nov. 25, 1933, complaining of incontinence of urine while standing, enlargement of the abdomen, weakness, and prolonged profuse menses. Her present history dates back at least six years when she was seen by a physician who told her that the enlargement was due to a pregnancy. Menstruation began at the age of fourteen years and has always been regular, the flow lasting from four to five days. During the past year the flow has increased in amount and duration and recently has given rise to the symptoms of secondary anemia.

The patient was well nourished but her mucous membranes were pale. She had dyspnea on slight exertion, even talking. The heart and lungs were normal. The abdomen was enlarged by a tumor mass arising in the pelvis and extending to the ensiform cartilage. This mass was hard and the percussion note over it was dull. There was tympany in the flanks. There was slight edema of the extremities. Pelvic examination showed that the tumor was evidently of uterine origin. The examination of the urine was negative. The blood Wassermann test was also negative. Her hemoglobin was 50 per cent, white cell count 10,000, and red blood cells 3,950,000.

The patient was given the usual preparation for operation and matched for transfusion. Three acceptable donors were made available. Under ether anesthesia, a large myomatous uterus was found extending to the diaphragm and not adherent, with subserosal veins 1 cm. in diameter. The entire uterus, both tubes and ovaries, and the appendix were removed by Dr. J. A. Sampson.

During the operation, after the blood supply of the uterus had been clamped or ligated, 500 c.c. of blood were obtained by me from the uterus by first inserting a No. 12 gauge needle into available large veins, including the large subserosal, the uterine veins, and the veins of the mesosalpinx, and then aspirating the blood by suction. Since the blood would not fill the veins as readily as if the arterial supply were intact, it was obtained by alternately applying suction and allowing the veins to fill by external pressure. The blood was citrated, filtered and given intravenously to the patient by gravity. After the removal of the uterus and cervix, 450 c.c. of blood were obtained by allowing it to drain from the tumor. This blood was not

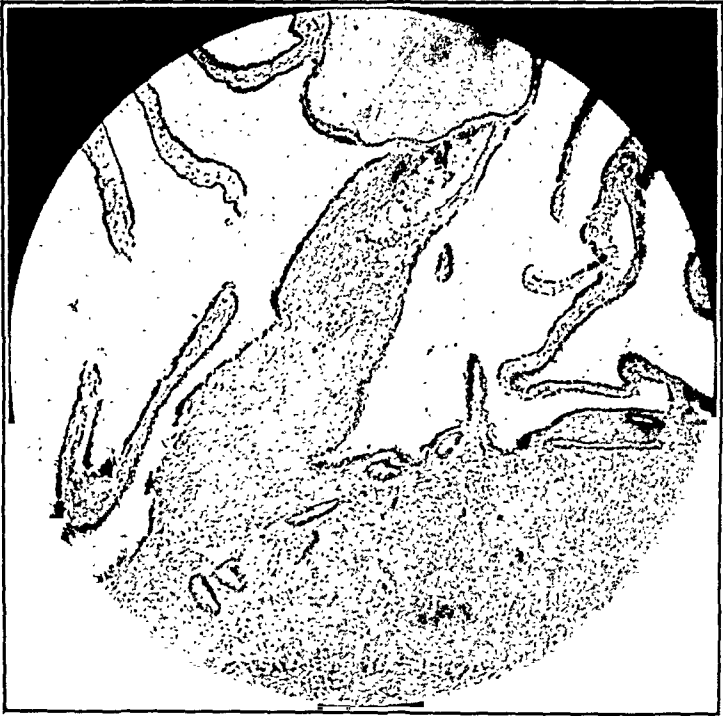


Fig. 2.—Section through the tumor proper, showing the papillary cystadenomatous character of the growth.

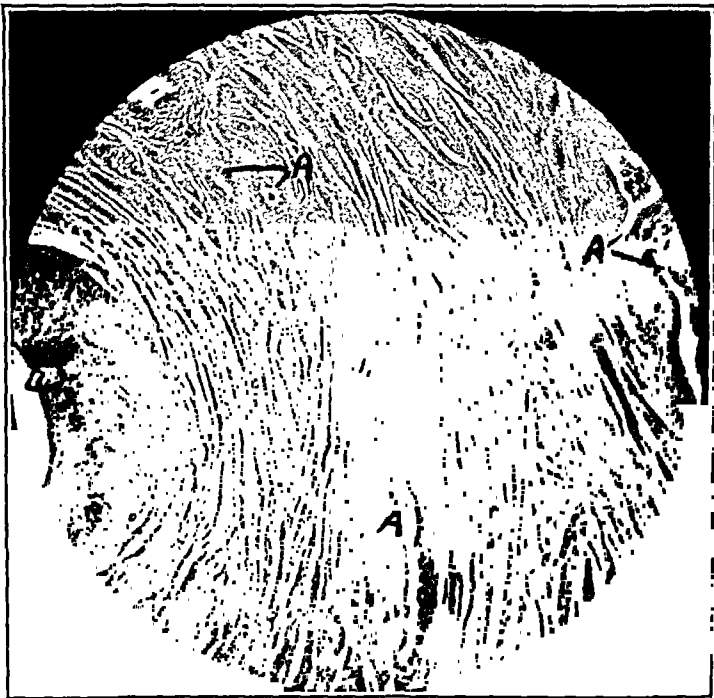


Fig. 3.—Section through the interstitial portion of the right tube. Note wolffian tubules (*A*) along the course of the fallopian tube, part of the lumen of which (*B*) appears in the section.

UTERINE PAPILLARY CYSTADENOMA OF WOLFFIAN BODY ORIGIN

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A SURVEY of the literature of the last twenty-five years reveals a prodigious number of articles under the headings of "adenomyoma" and "adenomyosis" of the uterus, but few cases, if any, of true papillary cystadenoma of the uterus have been described as such.

C. J., Porto Rican, thirty-eight years of age, married for fourteen years, was admitted to the Cumberland Hospital of Brooklyn on March, 1935, complaining of a mass in the lower abdomen for two years. She had no pain or other associated symptoms and was normal in every respect. Menstruation began at the age of fourteen. She was menstruating at the time of admission to the hospital and her last normal

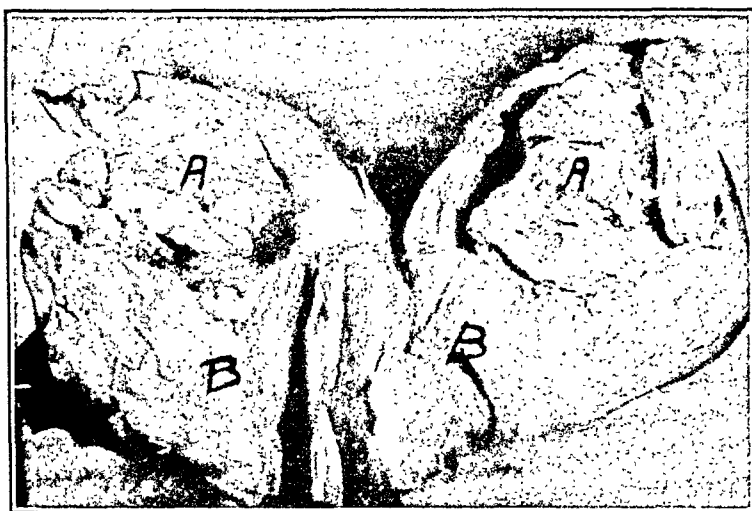


Fig. 1.—Gross specimen showing tumor (A) situated in the upper portion of the uterus (B).

period occurred a month previously. She had one pregnancy which ended in a spontaneous miscarriage (date unknown). Abdominal examination revealed a movable mass, about 9 by 12 cm., in the lower abdomen, arising from the pelvis, which by bimanual examination was apparently part of the uterus. No tenderness was noted in either the region of the mass or the uterus. The cervix was in the vaginal axis and the adnexa were not felt.

The blood Wassermann and the Aschheim-Zondek tests were negative. *Preoperative diagnosis:* Fibromyoma uteri. *Operative diagnosis:* Fibromyoma uteri and chronic bilateral tuboovarian disease. *Operation:* Supracervical hysterectomy, bilateral salpingo-oophorectomy. The wound healed by primary union and the patient made an uneventful recovery.

PATHOLOGIC REPORT

Gross specimen: (Fig. 1.) Consisted of uterus and adnexa. The uterine wall was smooth and ovoid in shape, soft in consistency, and the uterus measured 10.5 cm. in length, 7.5 cm. in width, and 5.5 cm. in anteroposterior diameter. The

DIABETES INSIPIDUS AND PREGNANCY

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DIABETES INSIPIDUS has been studied extensively, but infrequent mention is made of pregnancy as a complicating factor. It is not the purpose of this case report to analyze the literature in great detail. Momigliano¹ (1929) in an extensive monograph, collected a total of thirty-one cases from the literature to that date and reported two cases of his own. Since then, three further cases (Anselmino and Hoffman,² Artaud,³ Dietel⁴) have been reported. Findings of significance have been: (a) Consistent lack of relationship to possible pituitary lesions as demonstrated by x-ray changes in the sella turcica, (b) infrequent relationship to positive Wassermann, (c) rather frequent incidence of premature labor, and (d) uniform response to posterior lobe pituitary medication. The possible undesirable effect of extensive use of posterior lobe extracts during pregnancy, especially during the latter months of gestation, must be considered.

Diabetes insipidus may be present before the onset of pregnancy or the disease may make its appearance during gestation. In the latter state (diabetes insipidus gravidarum) subsequent to the termination of the pregnancy the diabetes insipidus may disappear or remain as a disease condition. The number of cases of diabetes insipidus present only during pregnancy and absent during the interim between pregnancies is rare. Thus the pregnancy is usually considered as purely coincidental. The case reported here was one in which conception took place about three months after onset of the diabetes.

G. van I., white, thirty years old, no constitutional disease, in good health. Measles was the only childhood disease. Patient married fourteen years. Seven previous pregnancies, three of which were observed in this clinic, all uneventful. Menstrual history normal, last regular period, Dec. 6, 1933. Flowed scantily in January, February, and March, 1934. This oligomenorrhea was an associated finding and was not due to pregnancy.

Weight averaged 152 pounds, present 182 pounds, entire gain since onset of present illness.

In the latter part of December, 1933, the patient noted a sudden thirst. From that acute onset, when she felt otherwise well, continued a severe polydypsia and polyuria. The intake and corresponding output was 12 to 14 quarts of fluid per day. The Jan. 9, 1934, menstrual period was very scant, an unusual occurrence with her, so she came to the Washington University Clinics for the first time on Feb. 16, 1934. It was thought that she was not pregnant. She was referred to the Medical Clinic because of the polydypsia and polyuria. An intranasal application of pituitary extract (posterior lobe) was administered with prompt relief for three hours. The patient was transferred to Barnes Hospital for observation and study.

Physical examination showed a well-developed, obese, white woman; short, broad physique, weight 182 pounds. Normal in all respects except as noted. Basal metabolism rate, 6 per cent, plus. Blood Wassermann, Kahn, Kline, negative. Average fluid intake before onset of medications was 7,000 to 14,000 c.c. a day with an average urinary output of 10,500 c.c. The specific gravity of the urine was 1.0005 to 1.005.

specimen was opened from the right lateral surface. The endometrial cavity was found to be a narrow, crescentic slit which extended to a height of 3 cm. from the lower pole. The cavity could be traced to the left tube, but on the right side it was lost and its continuity could not be established with the right tube.

An intramural, pale pink, cystic, trabeculated mass 5 by 6 by 4 cm. occupied the greater portion of the uterine body and fundus, and contained a large number of discrete cystic structures of varying size which were mucoid in appearance and were filled with a clear colorless fluid. The main wall was completely surrounded by myometrium and merged imperceptibly with it.

The tubes were thickened, cystic, and retort-shaped. The fimbriated ends were sealed. On section, the tubal lumina were found to contain a viscid, chocolate-colored content.

The ovaries were small, intimately adherent to the tubes, and on section presented a sclerotic appearance, with several small follicular cysts, and hyalinized corpora albicantes.

Microscopic: (Figs. 2 and 3.) The tumor was composed of interlacing cystic and papillary structures which were lined by epithelium, varying from low cuboidal to tall columnar, both ciliated and nonciliated cells, and supported by a stroma of muscle and connective tissue, but nowhere in the stroma could endometrium be demonstrated. Serial sections failed to establish continuity between the newgrowth and the endometrium. Sections through the interstitial portion of the right tube and including a small area of the cystic mass disclosed the interstitial portion of the tube, and there were in its vicinity numerous ducts and glandlike structures, varying in size and shape. They were lined by cells which were both ciliated and nonciliated and which varied from low cuboidal to tall columnar, directly imbedded in the muscle tissue of the uterus, with no communication with the tubal lumen. These structures were histologically recognized as epoophoron-like (wolffian body rests). A number of these ducts and glandlike structures were cystic, some were papillated and showed a striking similarity to the histologic picture of the uterine intramural newgrowth described above. The tubal walls presented a chronic inflammatory process. Sections of the ovary showed a chronic oophoritis and several follicular cysts.

DISCUSSION AND CONCLUSION

In the opinion of the authors, this tumor is probably of wolffian body origin. Notwithstanding Cullen's view that one cannot differentiate from the histologic picture a wolffian or müllerian origin of intramural cysts, the histologic picture of this newgrowth is apparently not of endometrial or tubal origin as evidenced by (a) the failure to trace continuity to either of these structures by serial sections as well as by (b) the absence of endometrial stroma in the tumor. On the contrary, the histologic picture of the newgrowth more closely simulates that of the epoophoron (wolffian body rests). This is in conformity with the observation of Ivanov, whose work shows the part played by the wolffian body in the formation of the uterine wall. Mercadé has demonstrated that the location of these wolffian body rests may be at the cornua, in the fundus, or along the lateral wall of the uterus. The structure and location of the mass in this case therefore may be considered a papillary cystadenoma of wolffian body origin and as such should be recognized as distinct from the adenomyomas of heterologous origin.

847 EASTERN PARKWAY
1325 EAST NINTH STREET

Various brands of whole posterior-lobe pituitary powders were administered by nasal insufflation.^{5, 6} Only one of these products proved to be consistently effective. Within a few days it was noted that four to five nasal insufflations daily controlled the thirst and polyuria effectively without any discomfort to the patient due to the treatment.

Soon after the condition was under control, the patient reported complete amenorrhea. The nasal insufflations were not interrupted. Throughout the pregnancy the patient was observed at intervals in the clinic and in the hospital. Blood chemistry, basal metabolism, blood volume, ophthalmoscopic examination, etc., were repeated at intervals with the hope that some pertinent information might be obtained (Table I).

After institution of posterior lobe nasal insufflation therapy, the fluid intake averaged by months was between 3,500 and 2,100 c.c., and the average urinary output was 3,400 to 2,100 c.c. Careful consideration of the daily intake and output record revealed no information of importance, except the return to a normal intake and output when pituitary extracts were administered after temporary cessation of treatment.

No untoward symptoms were noted until Dec. 11, 1934, at about the thirty-seventh week of gestation, when for the first time painful, irregular uterine contractions were noted following insufflation intervals. Not every insufflation was followed by uterine contractions, but the response was more marked as term approached. On Jan. 2, 1935, a normal 3,510 gm. baby was born spontaneously after an eight-hour labor. Absolutely no abnormalities in the character of labor were noted. The child, now two and one-half years old, is perfectly normal.

The patient, two and one-half years after termination of the gestation, is in the same physical condition as she was as soon as posterior lobe medication was begun. The diabetes insipidus is well controlled by posterior lobe pituitary nasal insufflation in approximately the same dosage and frequency of medication as previously.

SUMMARY

The history of onset of disease and clinical course is typical of diabetes insipidus.

Physical examination and laboratory findings are all within physiologically normal limits. This includes blood chemistry, blood volume, blood counts, basal metabolism, x-ray studies, ophthalmoscopic examination, and visual fields.

The patient was advised to use the posterior pituitary powder insufflations as liberally as necessary to control the disease. During the last six weeks of pregnancy, it is possible that not quite as much powder was necessary to maintain balance. This observation was entirely subjective and not marked enough to be of importance.

Not until the thirty-seventh week of pregnancy did the uterus respond to the medication by uterine contractions.

The baby, now two and one-half years old, is a normal child.

The patient at the present time requires essentially the same amount of medications as when observed during pregnancy.

The diabetes insipidus apparently was not influenced by the pregnancy.

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TABLE I. BLOOD CHEMISTRY

DATE	UNDER Rx	HB %	C.V. %	B.S. MG. %	N.P.N. MG. %	CL. MG. %	PROT. MG. %	CHOL. MG. %	FATTY		TOTAL LIPID MG. %	CA. MG. %	P. MG. %	BLOOD VOLUME			
									ACID MG. %	LIPID MG. %				HB. %	C.V. %	PLASMA VOLUME IN C.C.	BLOOD VOLUME IN C.C.
1934																	
3/11	No	--	--	89	32	---	--	---	---	---	---	10.2	2.9	---	---	---	---
7/11	Yes	96	42	105	32	601	5.8	---	---	---	---	---	---	---	---	---	---
8/20	No	83	39	108	24	613	6.0	263	316	579	579	---	---	83	39	3855	6319
8/21	Yes	89	40	94	30	601	5.9	250	341	591	591	---	---	89	40	3742	6233
8/30	Yes	86.9	39	92	39	572	6.8	364	678	1042	1042	---	---	---	---	---	---
12/18	Yes	80	38	86	30	607	7.2	262	663	925	925	---	---	---	---	---	---
12/19	No	80	38	89	25	607	7.2	258	583	841	841	---	---	---	---	---	---
(Postpartum)																	
1/10/35	Yes	95	42	103	42	601	5.5	308	752	1060	1060	---	---	---	---	---	---

right side of the chin, the external appearance was essentially normal. There were petechiae in the epicardium on the posterior aspect of the base of the heart and in the periosteum of the cranial bones. Numerous ecchymoses were found in the falx cerebri and the tentorium cerebelli, although the tissues were intact. The venous sinuses were normal, but the spinal fluid was blood tinged. The esophagus and the first portion of the jejunum were congested, but the remainder of the gastrointestinal tract was normal. The other organs were essentially normal.

Microscopic examination showed marked congestion of blood in the capillaries and in the small bronchi of the lungs. The alveolar ducts and the alveoli, which were not completely expanded, were filled with particles of amber pigment and a few



Fig. 1.

red blood corpuscles. Some of the pigment was in the cytoplasm of the large mononuclear cells in the alveolar spaces and in the interstitial tissues. The cells of the peribronchial cartilage also contained this pigment.

The spleen showed congestion in the pulp. There were congestion of blood in the capillaries and hemorrhages in the interstitial tissue of the pancreas. The liver also showed marked congestion of blood in the interlobular veins, the sinusoids, and in the central veins, and hemorrhages in the interstitial tissue. In the liver cells there were large drops of pale pink homogenous material. Numerous small collections of nucleated red blood corpuscles were scattered throughout the section. The kidneys showed the same picture of congestion of blood in the cortex and pyramide.

Neurologic examination by Dr. L. D. Stevenson of the Department of Neuropathology, was essentially normal except for clotted blood in the subarachnoid

FETAL DEATH DUE TO STRANGULATION DURING LABOR

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THE case herein described is reported because of the unusual findings associated with the death of the fetus.

The patient was a colored multipara of twenty-three years of age. She had had three previous full-term pregnancies, the children all living and well. She was first seen at the Berwind Clinic on Oct. 25, 1933, in the thirtieth week of her fourth pregnancy. The examination was essentially normal and the presentation was thought to be a vertex. The Wassermann reaction was three-plus, although it was negative one month previously. The patient did not return for further examinations.

On November 5, two weeks later, she was seen by a member of the staff because of the onset of labor. The membranes ruptured at 10 A.M. on that day, and the patient was having mild pains which did not continue. The cervix was thick and closed, and the presentation was a breech. After observation it was decided that the patient was in false labor.

True labor began at 8:30 A.M. on November 7, about forty-six hours after the rupture of the membranes. When first seen in her home at 10:10 A.M., the patient was in very strong labor. It was believed that the breech was presenting. The cervix was 6 to 7 cm. dilated and the presenting part was at the spines. No meconium was present. The fetal heart was extremely slow, around 60 per minute. The fetal distress was thought to be due to the strong contractions, and consequently open drop ether was administered. However, twenty minutes later the fetal heart was lost, and labor was progressing rapidly.

Fifteen minutes later the caput presented at the outlet. The head was in R. O. A. position but poorly flexed. It was essentially a breech presentation. As the chin was being delivered, both feet presented at the outlet, just under the chin. There were two loops of cord between the neck and the feet, but these were loose and easily slipped over the shoulders. The baby was then delivered in that position, with the feet delivering with the trunk. The fetal heart failed to respond to attempts at resuscitation.

The baby was a normally developed female weighing 3,000 gm. The lower extremities were flexed at the hips and extended at the knees, so that both feet were under the chin. On the right side of the chin the imprints of the toes could readily be seen. There was congestion of the head and neck, the upper eyelids being swollen with blood. The photograph was taken a few hours after delivery and shows the unusual posture as well as the edema above the neck. At the time of delivery it was felt that death was due to pressure on the neck vessels.

Microscopic examination of the placenta by Dr. H. F. Traut showed leucocytic infiltration of the chorion denoting placentitis and probable infection of the amnion. The villi were not absolutely characteristic although somewhat suggestive of syphilis.

Postmortem examination was done twenty-four hours after delivery by Dr. H. S. Dunning of the Department of Pathology. Except for the edema of the head, the hemorrhages into the upper eyelids, and the imprint of the foot on the

A SIMPLE, SAFE AND ECONOMICAL CORD CLAMP

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MANY types of instruments and appliances have been devised and used to replace ligation in the care of the umbilical cord of the newly born infant. Ligation is still the most commonly used but its popularity is obviously waning. Any successful method must provide complete asepsis, proper hemostasis, and normal wound healing. Several instruments based upon various mechanical principles have been used satisfactorily, some of which have yielded better results than ligatures. Because of the cost of most, if not all, of these instruments, it seemed desirable to make a cheaper clamp equally as effective.

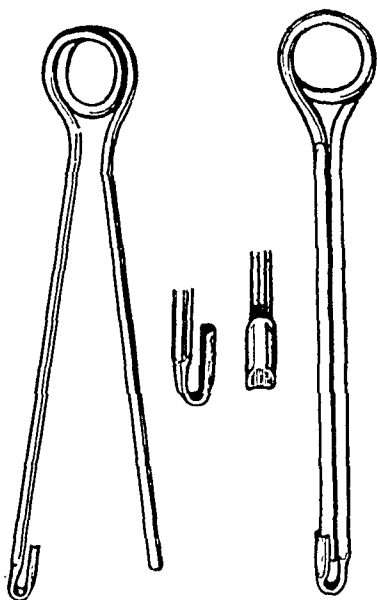


Fig. 1.

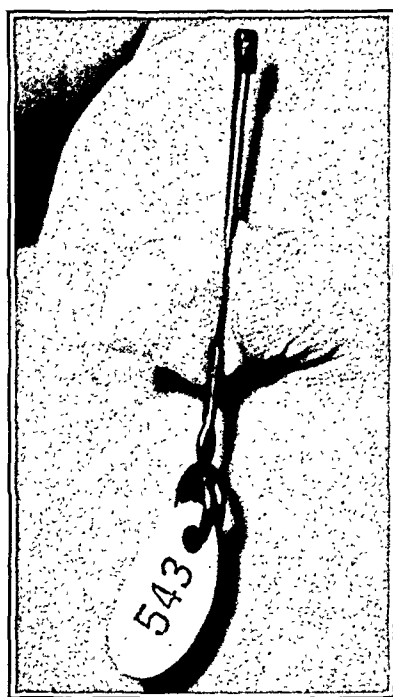


Fig. 2.

Fig. 1.—Perpendicular and horizontal views of the clamp.

Fig. 2.—Appearance immediately after birth with clamp locked in place. Within twenty-four hours the stump will be dry.

Such an apparatus should be safe, be simply constructed, be easily and quickly applied, and allow free inspection without manipulation. These requirements were fulfilled finally in a steel spring clamp. Rectangular strip steel could be substituted but to be equally as strong would have to be heavier and wider.

This clamp is constructed from one continuous piece of wire* (Fig. 1). The two arms make a direct contact with each other when they are closed, as they have a slight convexity toward each other. One arm is cut longer and bent backward on the proximal side and then grooved in such a fashion that it provides a good catch or lock. The double loop spring portion at the opposite end gives the necessary

*Mr. Angrabright of the Clinics' Machine Shop made the original models.

space encapsulating the pole of the right temporal lobe. No abnormalities of the ventricles, basal ganglion, internal capsule, the brain stem, or cerebellum were noted.

The positive pathologic findings were therefore extreme flexion of the lower extremities; hemorrhage into the upper eyelids; congestion of the head and neck; subarachnoid hemorrhage over the pole of right temporal lobe; congestion of lungs, liver, spleen, pancreas, kidneys, esophagus, and jejunum; ecchymoses of falx cerebri and tentorium cerebelli, and petechiae in the epicardium and periosteum of the cranial bones.

DISCUSSION

The clinical picture and findings at the time of delivery suggested that death was due to strangulation caused by the pressure of the feet on the neck vessels. The prenatal observations suggested a breech presentation, and this is supported by the unusual posture of the baby at the time of delivery. The pathologic findings are all consistent with this cause of death. Although at the present time there is considerable discussion as to just what the pathologic findings are in cases of strangulation, it is admitted by most pathologists that the findings above mentioned are usually present in those cases. Prematurity may be responsible for the petechiae noted in this case. Although the baby weighed 3,000 gm. and was 55 cm. in length, the presence of nucleated red blood corpuscles in the liver indicated prematurity. The fact that the baby was delivered two months prior to the expected date of confinement supports the diagnosis of prematurity. This of course would accentuate the findings due to strangulation.

Syphilis may have been responsible for the premature labor although the placenta did not show the characteristic findings. The Wassermann reaction was negative six weeks before delivery but was 3-plus four weeks later. (The patient has had two other pregnancies since then. In 1935 she received a course of anti-syphilitic treatment during pregnancy although the Wassermann reaction was plus or minus. A 4,000 gm. baby in good condition was delivered in April, 1935. In May, 1936, she was delivered of a normal 3,400 gm. baby and during that pregnancy the Wassermann reaction was negative.)

Because of the findings, and in the absence of any other definite cause of death, it can be assumed that this mortality was due to strangulation during labor.

From an obstetric point of view this case presents a possibility that might occur with external version. It is surprising that this has not been noted in such cases. This may be due to the fact that the patient had premature rupture of the membranes and that the spontaneous version took place shortly before labor.

6

Rosselli, C.: Dilatation of the Pregnant Uterus, According to the Law of Sfameni, *Monitore ostet. ginec.* (Bologna) 7: 529, 1935.

The author refers to the writings of Sfameni and others relative to a "diastolic" state of the uterus during pregnancy. He shows that the histologic structure of the wall of the pregnant uterus is not like that of an organ subjected to positive pressure exerted by the growing ovum, as is generally believed, but that of an organ which expands by itself, by a process of active dilatation, a diastole, as Sfameni has asserted for the past thirty years.

AUGUST F. DARO.

Special Article

HUGH LENOX HODGE

A MASTER MIND IN OBSTETRICAL SCIENCE

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MEDICAL textbooks of a former generation for the most part are interesting only from the historical point of view. There are exceptions, however, for rarely we find among these faded volumes one which is so masterful in its delineation, so fraught with the truths of experience that we are able to view in clearer relief the real stature of a great mind of other days. Such a work is *The Principles and Practice of Obstetrics* by Hugh Lenox Hodge, published in Philadelphia nearly three-quarters of a century ago. Hodge's work is the true progenitor of our modern American textbooks on this subject. Indeed, many of its fine lithographic illustrations have not been equalled, and much of its facility and clarity of description has not been surpassed. "This volume," wrote Whitridge Williams, "which is a model of conscientious observation, is undoubtedly the most original work which has appeared in America, and with few modifications is as valuable today as when first written."

• If we review the history of obstetrics in our country during the middle years of the last century, eminence seems to center around two names, Charles D. Meigs and Hugh L. Hodge, both of Philadelphia. These two leaders in medicine were unrivaled in their influence as teachers of obstetrics, and although the former was probably the more spectacular personality, the contributions of the latter evince a soundness and originality that we are more prone to associate with true greatness.

Hugh Lenox Hodge was a descendant of Andrew Hodge, a Scotch-Irish Presbyterian who emigrated to America in 1730. With two brothers he settled in Philadelphia, entering the mercantile business. A son of Andrew Hodge and father of Hugh Lenox Hodge, was Hugh Hodge, born in 1755 and graduated from Princeton College in 1773. Shortly after this he was apprenticed in medicine to Thomas Cadwalader, a noted physician and one of the first lecturers on anatomy in the new world. During the Revolution Dr. Hugh Hodge became an army surgeon, was captured by the British and liberated on parole through the intercession of General Washington. After the war he settled in Philadelphia and in 1790 married Mary Blanchard of Boston. Hugh Hodge

flexibility without loss of tension. The two arms are compressed into proper alignment. The various dimensions are as follows: The diameter of the wire 17 to 18 B & S gauge; length over all 6 cm. ($2\frac{3}{8}$ in.); diameter of the coil spring 1.2 cm. ($\frac{7}{16}$ in.); the length of the hook or catch 0.4 cm. ($\frac{3}{8}$ in.); length of arm 4 cm. ($1\frac{1}{2}$ in.). These dimensions provide ample room for application without contamination, yet the clamp is covered easily by the cord dressing, thus avoiding the dangers encountered with the larger, broader, heavier, and longer instruments.

After clinical tests were made with the "model" clamps and their value was demonstrated, a sufficient number of clamps of stainless steel wire were obtained* for routine use. Since Nov. 15, 1935, to the present time over 1,500 unselected babies have had their cords treated by this method. Since the systolic blood pressure of newly born infants probably does not exceed 100 mm. mercury and these clamps prevent vascular leaks with pressures in excess of 250 mm. mercury and do not slip, there should be no bleeding. This contention is verified by complete hemostasis in all applications.

The clamp is applied and locked immediately outside the margin of the squamous epithelium. The cord should then be cut 2.0 to 2.5 cm. ($\frac{3}{4}$ to 1 in.) above the clamp. It is important that this much tissue be left as a margin of safety (Fig. 2). The cord dressing is easily applied. No instrument is used in applying the clamp, and it may remain on until the cord stump falls off. However, if one desires, the clamp may be removed after twenty-four hours. Since it is covered with the dressing, the baby may be turned, moved and handled safely and without risk of injury yet the stump may be inspected at any time by merely removing the dressings. The cord dries promptly and usually drops off in three to seven days. Furthermore the healing process has not only been enhanced but also has been extremely satisfactory.

These stainless steel clamps have been used repeatedly without showing loss of quality. They are simple, safe, dependable, and very economical.

A more detailed report will be made later.

*The American Spring Coil Company, Muskegon, Michigan, made these clamps.

New York on the "Julius Caesar" on Sept. 8, 1818, and five months later arrived in India. Unlike his preceptor, however, the voyage was a financial failure although his rich experience in the cholera hospitals at that time was to stand him in good stead during the cholera epidemic in Philadelphia in 1832. On his return to America he opened an office on Walnut Street and soon after was elected physician to the Southern Dispensary and to the Philadelphia Dispensary. In the summer of 1821 he was selected to teach the anatomy class of William E. Horner who was absent in Europe. Two years later he was appointed to the lectureship on Surgery in Chapman's summer school, which later became the "Medical Institute." This last appointment says Hodge was a turning point in his life and led him into medical teaching as a career. Not long after this an unexpected change in his career took place. Because of a gradual failure in vision he was led to abandon surgery and turn his attention to another field. He chose obstetrics.

In 1828 Hodge married Margaret Aspinwall, the daughter of John Aspinwall, Sr., of Flushing, New York. To them were born seven sons, four of whom became clergymen and one who became a surgeon.

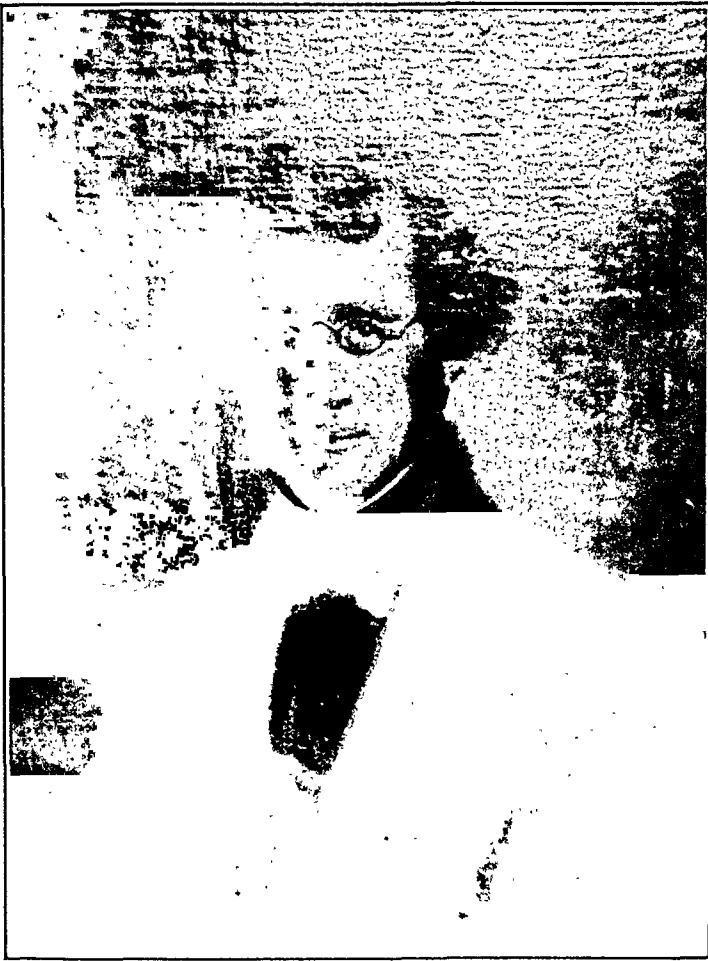
When Thomas Chalkley James resigned his Professorship in Obstetrics at the University of Pennsylvania in 1834, William Potts Dewees was chosen his successor. However, because of ill health the latter was forced to withdraw and the chair became vacant. The leading candidates for the position were Hugh L. Hodge and Charles D. Meigs. In his innate modesty Hodge refused to exert himself for the position, much to the annoyance of friends who were working for him. The young candidate was finally prevailed upon to call upon the trustees. At his first visit to a very eccentric friend, after stating his errand he was told "young man, I should have thought better of thee, hadst thou not come." This was the first and last visit of that nature that Hodge made. Nevertheless his friends continued to work and the campaign, for such it was, resulted in his election. He now joined the medical faculty with Nathaniel Chapman, Robert Hare, William Gibson, William E. Horner, Samuel Jackson, and George B. Wood.

His first term in the chair was not an unmixed blessing, for it was customary for the new professor to pay the trustees an entrance fee of \$600, and furthermore these gentlemen had promised Dewees that the proceeds of the course after expenses had been deducted should revert to him. However, Hodge's connection with the University soon brought him a lucrative practice, patients coming from great distances, particularly from the Southern States.

His vision which had insidiously failed by 1850 had become so impaired that he was unable to read ordinary written manuscripts. Ten years later when his volume *Diseases Peculiar to Women* was published, it proved to be the last effort made with his pen. In addition to this affliction, the years of the Civil War showed a great diminution in his

played a prominent part in the terrible epidemic of yellow fever in 1793 and 1795, and it is probable that his labors at that time hastened his early death in 1798.

Hugh Lenox Hodge was born in Philadelphia, June 27, 1796. His early education was gained under Mr. Thompson at the grammar school of the University of Pennsylvania and later at boarding schools in Summerville and New Brunswick, New Jersey. At the age of fifteen years he entered the sophomore class at Nassau Hall, Princeton. Here at this



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time also as a student was his only brother, and in order to defray expenses the mother moved to Princeton and took four other students into her family.

In September, 1814, Hodge graduated and immediately began the study of medicine in Philadelphia under the celebrated Caspar Wistar, then at the height of his fame. In August, 1818, at the age of twenty-two he was graduated a doctor of medicine from the University of Pennsylvania. At this time it was his desire to spend a year of study in Europe, and following the footsteps of his teacher T. C. James he enlisted as a ship surgeon on a vessel bound for Calcutta. He sailed from

toward the lumbar vertebrae, of course the spine and back are directly anterior . . . in a few cases, the continuance of the third position may be maintained by some peculiar elongated form of the superior strait, so that the anteroposterior diameter may be comparatively long."

At a time when cesarean section was almost universally condemned, Hodge's view had a real prophetic note; he writes, "The hope, also, may be entertained that if the patient be in good condition mentally and physically, and if the deformity of the pelvis be ascertained previous to the recurrence of labor, so that suitable preparations can be made for the operation, gastrohysterotomy will prove far more successful than in times past, and, perhaps may be justified even in cases of moderate deformity, when the child is alive, for the purpose of preserving its life as well as that of its mother."

There is no doubt that Hodge was an outstanding authority in deformities of the pelvis and his evaluation of external pelvimetry as a method of diagnosis sounds indeed a modern note as witnessed by the following: "Many physicians have placed great confidence in the external measurements of the pelvis; but this is liable to many errors, even from the varying conditions of external tissues, and can in no sense give any exact idea of the form or dimensions of the pelvic cavity."

Hodge opposed Holmes' views with regard to the contagiousness of puerperal fever, but unlike his vehement colleague, Meigs, he raised no animosity in the heart of the young professor at Harvard. "His remarks," Holmes observed, "are unobjectionable in tone and language, and may be read without offence." In Hodge's *Principles and Practice* the whole subject of childbed fever is treated in a minimal way and no reference is made to the controversy which had raged a dozen years prior to its publication. Hodge is said to have been opposed to anesthesia in childbirth but this is an error. He was apprehensive of the use of chloroform, but his words on the subject of anesthesia show him to be essentially an advocate of its use. His views are summed up in the following quotation:

Often a slight anaesthetic influence may be sufficient to moderate without destroying sensibility, so that labor progresses regularly, without any considerable pain or disturbance. This is all that is necessary, except in a few, perhaps very few, obstetric operations. The author, therefore, coincides in belief with those who insist that the patient ought not to be entirely unconscious. The practitioner should have command of his patient, that he may direct what sensations are to be resisted, and what should be encouraged; when the bearing-down efforts are desirable, and when they should be remitted; and, of course, the woman should be in a condition to advise her attendant as to the occurrence of any unusual pain, morbid sensation, etc. There are a few cases of course, where complete anaesthesia may be essential.

In describing the conduct of the third stage of labor, Hodge anticipated the maneuver that we associate with the name of Credé, he

practice particularly among his Southern clientele. Following his course in 1862 and 1863 because of failure of vision he resigned his professorship and became emeritus. He now devoted his time to the writing of his great work the *Principles and Practice of Obstetrics* and in producing this he had to rely on an amanuensis and on editorial assistance from his son.

From the professional viewpoint the remainder of Hodge's life does not have peculiar interest. A biographer says "sixty-seven years old, he did all the professional work which could be done without eyes. The poor and the students could still count upon finding him in a serene mind, tender and sympathetic with a loyal unswerving trust in God." In 1871 his Alma Mater in medicine honored herself and him by bestowing the degree of Doctor of Laws and in 1873 on February 23 after a day's illness with cardiac failure he passed on.

The outstanding and important contributions of Hugh Lenox Hodge are found in his *Diseases Peculiar to Women* (1860) and *The Principles and Practice of Obstetrics* (1864). In the former is found an excellent description of the appliance which added greatly to his fame, the well-known Hodge pessary. The evolution of this instrument was the result of many years of experimentation during which countless shapes were tried and many materials used. Hodge was one of the first to use vulcanite after its invention by the pioneer Goodyear. The important modification introduced by him consisted in making the ring oblong instead of circular and so curved as to correspond to the curvature of the vagina. During the period of the evolution of this instrument, a biographer writes, "Sitting one evening in the University his eyes rested on the upright steel support designed to hold the shovel and tongs, which were kept in position by a steel hook, and as he studied its supporting curve, the longed-for illumination came and the lever pessary was the result." In order to evaluate the importance of this mechanical device as a boon to suffering womankind, we must remind ourselves that plastic surgery for female ills was in Hodge's day practically unknown.

Hodge's great contribution to medical literature was his *Principles and Practice* first published in 1864. Because of necessary space limitation, we can but figuratively glance into the pages at this time, but even this will give some idea of the true greatness of his contribution to obstetrics. The fine historical essay in the preface shows the author's familiarity with the authors of his day and with those who have gone before. Under "anatomy of the pelvis" he gives a fine description of his theory of parallel pelvic planes which, though of little practical use today, does show how familiar the author was with the architecture of the pelvis. Hodge was even familiar with variations in this architecture and their influence on labor as is witnessed in the following quotation. Under "occipitopelvic position" he writes, "In this position (the third of Baudeloque) the occiput is toward the pubis and the superior part of the os points

The foregoing excerpts from Hodge's important treatise bear out the statement of Williams as to its value as a fundamental work of reference. The real inquiring student today should not overlook the many practical suggestions to be found therein. Perusal of its pages reveals the writer as a master of his subject, but there is other and perhaps finer inspiration to be gained from Hugh Lenox Hodge than one finds in his written word. The fine fortitude which he displayed in carrying on his life work under his terrible affliction shows his true greatness. His life exemplified those qualities which we associate with mastery of life and superiority among men.

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Maternity care propaganda to be helpful must be conducted on lines of reassurance and not of menace. The susceptible nervous system of the pregnant woman is readily impressed by a recital of possible complications even to the extent of what has been termed anxiety neurosis.

An essential objective to ensure the success of maternity services is to gain the confidence and support of women generally. The postnatal care should be the corollary of the antenatal clinic, in view of the fact that 40 per cent of the cases attending gynecologic out-patient departments have a causal relation to obstetrics.

The midwife may make or mar the success of any maternity service.

A national maternity service which excludes the general practitioner from its responsible personnel is impossible and unthinkable. The consultant is essential to a maternity service. He consults with the general practitioner.

The hospital is an indispensable adjunct of a maternity service, provided the maternity beds are kept well separated from the mixed hospital. The home is infinitely safer than the carelessly conducted hospital. The availability of analgesia or anesthesia for parturient women is a factor in gradually increasing numbers applying for institutional care. The conduct of and the equipment for home deliveries will remain the center of the whole problem and will, in the main, control the mortality and morbidity rates.

For a national service both central and local advisory bodies with suitably representative membership and with responsible status would be necessary.

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writes, "Should there be any unusual delay, the practitioner may facilitate the contraction of the uterus by placing his hand through the medium of the relaxed walls of the abdomen, over the fundus of the uterus, and by making firm pressure direct the whole organ towards the superior aperture of the pelvis."

How well Hodge anticipated many of our modern views with regard to labor mechanism is shown by the following. "In describing the mechanism of labor; it will be found that the head of the infant descends from the superior strait to the floor of the pelvis very nearly in a straight direction, corresponding to the axis of the superior strait. The top of the head which was originally parallel to the superior strait, does not materially alter its direction until it comes in contact with the coccygeal region. It will be found also that the important process termed extension does not commence until the descent just mentioned, be nearly completed; indeed that it cannot occur until the top of the head reaches the perineum, and the suboccipital region passes under the arch of the pelvis."

Hodge was a great believer in the forceps and wrote, "A very large proportion of the vesico-vaginal fistulae, too frequently to be met with, result, *not from the use, but from the neglect of the forceps.*" His own modification of this instrument embodied many advantages over most of the instruments of his day; his endeavor was to "embrace all the advantages, without the defects of the Baudeloque forceps." His directions concerning the forceps may be quoted as a model of instruction.

Second rule to be observed is, to operate very slowly, and in the direction of the axis of the pelvis. The object of the accoucheur is to imitate nature as far as practicable; in spontaneous deliveries, in contracted pelves, labor is necessarily tedious; the compression to which the head is subjected is always gradual allowing time for the yielding of the commissures, the overlapping of the bones, the elongation of the head, and the consequent alteration of the form of the contour of the cranium. Hence, the forceps being applied, very slight compression and traction should be made at first; the patient should be encouraged to make her bearing down efforts, and the practitioner should afford moderate assistance during the existence of a pain. As soon as this intermits, pressure should be removed from the handles, so as to free the head as much as possible from compression. . . . It should never be forgotten that the forceps should be regarded as a mere addition or substitute for the natural powers by which the child is expelled.

In conclusion, the following quotation from his chapter on labor is significant of the soundness and truth of his doctrines.

These observations, the truth of which must be palpable, justify the declaration, that every labor should be under the supervision of a scientific accoucheur, in order that there may be no interference, direct or indirect, with the natural process of delivery. It is the business, therefore, of the practitioner carefully to watch the whole process of labor, to ascertain whether it is perfectly regular, and to detect any, even the least deviation from the natural process, that timely assistance may be rendered.

Some means other than radium applied to the cervix must be employed in the attempt to treat adequately the outlying tumor-bearing regions, such as external irradiation by roentgen rays. Taussig⁴ performs lymphadenectomy after irradiation, or at the time radium is used. The radium treatment consists of a cervical application, or the insertion of gold seeds into the regions occupied by the various lymph glands. In some instances both methods may be employed. The best results have been obtained in Group II patients (*League of Nations Classification*), to whom that procedure is now limited.

The amount of external irradiation that must be delivered in the attempt to treat adequately the disease in the outlying tumor-bearing regions will produce an erythema of a rather marked degree in the irradiated skin fields, and some constitutional reaction in the patients receiving the dose. Due to the fact that the parametrial regions and the adjacent lymph glands are involved in most instances, the administration of roentgen rays is just as essential as the application of radium to the cervix. It is important, therefore, that the tissue damage at the site of the application of radium be limited to a degree that will not interfere with the administration of external irradiation. The use of x-rays in conjunction with radium applied to the cervix delivers greater doses to points throughout the pelvis than could be obtained from either method alone. By this means the volume of tissue receiving a lethal dose will be increased, whatever the method of applying radium to the cervix. The degree of increase will depend upon the amount of roentgen radiation reaching the tumor.

There are certain advantages to be gained if the treatment of a cervix case is begun with x-rays. By this means any existing infection will be diminished, which, in turn, will reduce the degree of reaction and the incidence of complications from the radium treatment given at a later date. Furthermore, the application of radium may be facilitated by regression of the size of the primary lesion.

Roentgen treatment can be administered in single exposures to each pelvic field, or a divided dose technic may be used. The latter procedure is not always practical for patients who have very advanced disease, and a marked amount of pelvic inflammation. For the average patient it has been found that from 2,000 to 2,400 roentgens (measured in air) can be delivered safely to each of four areas (2 fields on the anterior surface of the pelvis, and 2 on the posterior), if administered over a period of from twenty to thirty days.⁵ A six-field technic (2 on the anterior surface, 2 on the posterior, and 1 on each lateral aspect of the pelvis), with a 70 cm. target-skin distance, has been found to deliver a distribution of radiation that is best suited to the treatment of cervix cancer.⁶ If six fields are irradiated it may be necessary in some instances to reduce the total dose given each area to 1,500 roentgens, when the treatment is administered within a period of about three weeks.⁷ In the average patient each method will deliver from 2 to 3 threshold doses throughout the tumor-bearing region. The administration of large amounts of external irradiation is particularly important in the treatment of carcinoma of the cervical stump.² In the absence of the uterine corpus it is difficult to make a satisfactory application of radium.

It is essential that patients be observed at frequent intervals during a course of divided dose treatment. The regression of the primary lesion should be observed carefully. In some instances, due to the marked shrinking and stenosis of the cervical canal, it may be necessary to

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

IRRADIATION OF MALIGNANT DISEASES OF THE FEMALE GENITALS

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THE introduction of radium and roentgen rays for the treatment of malignant disease has found widespread application in lesions of the female generative tract. The success of these agents has led unfortunately to their abuse in many instances, and it is essential not only that a study be made of the indications presented by each patient but that a definite knowledge be acquired of the manifold effects and complications which attend their employment.

In the treatment of malignant or suspected lesions, a biopsy is necessary before radiation is administered. Removal of a small piece of tissue from a suspicious lesion of the cervix rarely produces bleeding that cannot be controlled easily. Curettage should be performed in all cases of abnormal bleeding from the uterus. A more formidable operative procedure may be required for obtaining a biopsy specimen in cases of ovarian tumors, or other deep-seated lesions. The histologic appearance of a tumor may have an important bearing upon the method of treatment, as well as the prognosis. Some lesions may be treated best by surgery alone. For others radiation may be the method of choice. In many instances both radiation and surgery are employed.

CARCINOMA OF THE CERVIX

Carcinoma of the cervix is a disease that may be considered as moderately radiosensitive. In most clinics surgery has been abandoned for patients with that disease, and treatment is given by radiation alone. The degree of radiosensitivity is difficult to determine, due chiefly to the destructive doses generally employed. However, there is evidence that at least 6 to 8 threshold doses must be distributed throughout the primary lesion to control the disease in that region.^{1, 2} Radium applied to the uterus alone will not deliver a lethal dose to points located at distances greater than 3 or 4 cm. from the cervical canal. This has been shown diagrammatically by charts illustrating the distribution of radiation for different methods of applying radium to the cervix.³ No single method is suitable for the treatment of all patients, and in some instances it may be impossible to make a satisfactory application of radium. The most suitable distribution of radiation will be obtained from an intra-uterine tandem combined, whenever possible, with some method for delivering radiation into the vaginal fornices lateral to the cervix. The so-called colpostat is used most frequently for that purpose.

20 to 22 per cent. (For carcinoma of the cervical stump the cure rate is only about 14 per cent.²) It is agreed generally that advance in the treatment of cervix cancer will be made by improving the methods for administering external irradiation, rather than by changes in technics for applying radium to the primary lesion.*

Schmitz¹¹ has published statistics showing an improvement in results for the changes made in his technic of irradiation over the past twenty years. The absolute curability for gynecologic carcinomas was given for various periods during which particular methods and specified doses were used. For the most part the changes were related to the administration of roentgen radiation. The first improvement in results was noted after 1921 when he began to use 200 kv. x-rays. There was no change in the radium dose of 3,000 mg. hr., which was administered by a single application. The second improvement in results occurred after 1926, when a divided dose technic was begun. The patients were irradiated through 2 to 4 skin fields until 1,375 to 1,800 roentgens had been delivered to each area. In some instances the radium dose was increased to 4,800 mg. hr., which was administered in three applications of 1,600 mg. hr. each that were given at intervals of eight days. Since 1933, he has used voltages ranging from 500 to 800 kv. Treatment has been administered by fractionated doses through 2 or 3 skin fields until 3,000 roentgens were delivered to each area. It is interesting to note that since the use of voltages of that order, he has decreased the radium dose to 1,200 mg. hr., and in some instances radium treatment has been omitted. The present method has not been in use for a time sufficient to permit observation of the results over a five-year period. However, he compared the preliminary results obtained within eighteen to thirty months after irradiation for all of the methods. Those values indicate that the results from the present technic will show improvement over those obtained from preceding ones. The improved results from external irradiation cannot be attributed to a change in quality alone. There has been a definite increase in the total dose delivered to each field, as well as in the amount reaching the tumor. Schmitz states that the value of 800 kv. x-rays can be determined only when the percentage of five-year cures is known. He adds that both radium and 200 kv. x-rays have proved to be of definite value, and will continue to be used. The greater voltage may be indicated in the treatment of large deep-seated lesions that cannot be irradiated adequately by the methods used most frequently at the present time.

CARCINOMA OF THE CORPUS

Surgery has proved to be an efficient method of treatment for early cases of corpus cancer. However, all patients with operable lesions cannot be treated by hysterectomy, because the disease tends to occur in elderly women. Age alone may not contraindicate an operative procedure, but there are frequently associated conditions that increase the risk considerably. Furthermore, there is evidence that hysterectomy

*It should be noted that no mention has been made of the use of interstitial irradiation (seeds, needles, etc.) in the treatment of cervix cancer. Methods employing interstitial sources have not been employed generally, but Ward and others have for a number of years used needles inserted into the cervix in conjunction with an intrauterine tandem. Since this paper was written there appeared a publication by Pitts and Waterman (*Surg. Gynec. Obst.* 64: 30, 1937). They used weak needles several centimeters in length implanted into the paracervical and parametrial tissues (in conjunction with an intrauterine tandem) for large doses delivered at low intensities over periods of five days or longer. Their five-year statistics are probably the best that have been obtained for cervix cancer in this country.

interrupt the external irradiation and apply radium. The reappearance of actively growing tumor noted in serial biopsies taken within the first two weeks following roentgen treatment indicates that, whenever possible, radium should be applied within that period.¹

The average intrauterine tandem used in the treatment of cervix cancer consists of 2 capsules. The strength of the lower capsule (cervical portion) is usually about twice that of the upper one. The tandem should be applied so that it is surrounded completely by the cervix with the lower end about level with the external os, or the most dependent portion of the primary lesion. Various intravaginal applicators can be used also, depending upon the gross character of the lesion in question. After the application the vagina is distended with gauze packing to increase the distance of the bladder and rectum from the radium in order to protect those structures from excessive doses. An indwelling catheter can be used to keep the bladder collapsed so that it will receive a minimum of exposure.

The full amount of the radium treatment may be administered by means of a single application, or, as was noted for x-rays, the total dose may be divided into several treatments given a few days apart. For a number of years Healy^{2, 8, 9} has delivered the full amount of radium radiation within thirty-six to forty-eight hours. He believes that an intrauterine tandem should not be left in place for periods longer than twenty-four hours without being removed and cleaned. Due to the presence of bacteria, prolonged applications may lead to complications from infection. Radium is applied within seven to ten days after the completion of a cycle of external irradiation. One of several intravaginal applicators, usually the so-called bomb, is directed toward the cervix, or into the lateral vaginal fornices for doses of 1,500 mg. hr. in each position. Due to excessive reactions he has, during the past few years, employed the intravaginal applicator in one position only, which is usually against the cervix. On the following day a tandem is inserted into the uterus for a dose of 3,000 mg. hr. The tandem is of sufficient strength to deliver that amount of radiation within about twenty-four hours. Six weeks after the radium treatment the cycle of x-rays is repeated, unless a divided dose technic had been employed for delivering a large amount of roentgen radiation before the application of radium.

At the Radiumhemmet (Stockholm) the radium treatment is divided usually into three applications. The first two are separated by an interval of one week, and the last is given three weeks later. Complete treatment, therefore, requires about four weeks. Heyman¹⁰ uses a tandem in combination with various cylindrical or flat intravaginal applicators. At each treatment the average dose for the tandem is 800 mg. hr., and for the intravaginal applicator is 1,500 mg. hr. After complete treatment about 2,400 mg. hr. will have been delivered by the tandem, and about 4,500 mg. hr. by an intravaginal applicator. For a number of years external irradiation was not employed in every instance. Since 1929 all patients with cervix cancer have received roentgen or telerradium radiation. Heyman states that the combined treatment has resulted in an improvement in results over those obtained from radium applied to the cervix alone.

It is interesting to note that the various technics employed for applying radium to the cervix at the Memorial Hospital (Healy), the Radiumhemmet (Heyman), and at other institutions, have produced about equal clinical results. The absolute five-year cure rates have ranged from

tubes into the peritoneal cavity. There is also the danger of perforating the uterine wall if pressure is made during the insertion of radium against a portion of the myometrium that is infiltrated by the disease.

To begin treatment with a course of x-rays would seem to be equally applicable to corpus cases as to cervical lesions. Among patients with bulky tumors distorting the cavity so greatly that a suitable application of radium cannot be made, a preliminary course of x-rays will facilitate the intrauterine treatment by reducing the size of the lesion. Furthermore, the danger of forcing viable cancer cells through the lumina of the tubes should be reduced. The combination of x-rays and radium will deliver greater doses to points throughout the pelvis than could be obtained from either method alone. In patients who are not to be operated upon, a more marked effect may be obtained from the external irradiation if a divided dose technic is used. If hysterectomy is to be performed, it seems desirable to limit the roentgen treatment to single exposures to each pelvic field.

For the radium treatment the active length of the intrauterine application should extend from the external os to the top of the fundus. The volume of tissue that will receive a lethal dose from a tandem (capsules end to end in a straight line) is not great. This has been shown histologically by the irregularities in radiation effect noted in various portions of the same uterus.¹⁵ Any method that will distribute the radium more widely throughout the cavity will improve the distribution of radiation. Hurdon and Chambers,¹⁹ Held,²⁰ and others have published diagrams showing the probable zone of effect for several methods of inserting radium into the uterus. Dietel²¹ has devised an intrauterine applicator by means of which capsules within the cavity can be arranged in a triangle, or in a so-called "bouquet." Heyman¹⁰ fills the uterine cavity with containers of various sizes that hold radium sources. Schmitz²² uses an adjustable "Y"-shaped applicator.

The average dose of radium employed in the treatment of corpus cancer ranges from 3,500 to 4,500 mg. hr. The application may be made during the first two weeks following external irradiation. For a number of years, Healy^{16, 17} has employed both radium and x-rays in many patients before the uterus was removed six to eight weeks later. In more than 50 per cent of the removed uteri, there was no evidence of viable cancer. If there is a possibility that some portions of the disease have not been irradiated adequately, hysterectomy should be performed, whenever practical, before recovery has taken place. Cellular alterations of the tumor appear within a few weeks. Additional data may indicate the time at which the maximum radiation effect is produced, and the rate at which the tumor recovers from a sublethal dose. The optimum time for hysterectomy would be after the greatest degree of radiation change, and before there was recovery from inadequate doses.

CARCINOMA OF THE EXTERNAL GENITALIA

The malignant lesions of the external genitalia are chiefly epidermoid carcinomas of an adult type that are relatively radioresistant. The disease tends to occur in elderly women among whom the tissues about the vulva are easily damaged, and usually show abnormal changes that are already present. Those regions will not tolerate the amounts of radiation required in most instances. As a result, the use of radiation has usually been limited to patients who were inoperable due either to the extent of the disease or some associated constitutional condition.

alone is inadequate for all patients with operable lesions. It has been demonstrated that a definite relationship exists between the histologic structure of the tumor and the end-results.¹²⁻¹⁴ In the well-differentiated lesions a high percentage of cures has been obtained. Practically none of the patients with anaplastic varieties of carcinoma have survived if treated by surgery alone.

The influence of the histologic type upon the prognosis, and the large number of patients not suited to surgery due to associated constitutional conditions, have led to a greater use of radiation in the treatment of corpus cancer. Some authors advocate radium and x-rays for all cases of this disease.

For evaluating surgery and radiation several reports¹⁵ have been published showing a comparison of the average five-year results in collected statistics. For all cases treated by irradiation, including both operable and inoperable lesions, cure rates of from 32 to 36 per cent have been shown. Among patients with operable lesions, from 47 to 54 per cent have survived the five-year period. In every large series the cures from hysterectomy have been from 56 to 59 per cent. It is interesting to note that among patients who might be considered suitable for surgical treatment, Heyman¹⁰ has reported a relative cure rate of 64.3 per cent for irradiation alone.

It is not essential that all patients be treated by only one method. In many clinics both radiation and surgery are combined in some instances. Postoperative irradiation has been used extensively. Preoperative treatment has been employed less frequently, and it is feared by many that the use of x-rays or radium would increase the technical difficulties of an operation performed at a later date. This has not been the experience of Healy.^{16, 17} He compared the effect of radiation administered before and after hysterectomy in 24 patients with adenocarcinoma, Grade 3. Fifteen of the patients were irradiated before the uterus was removed. Of this number 60 per cent were cured. In 9 patients postoperative treatment was given, and only 33 per cent survived. It should be noted that most of the patients who were treated before operation received an intrauterine application of radium in addition to x-rays. Those who were given postoperative irradiation were treated by means of roentgen rays alone.

In a collected series of 91 patients who received an intrauterine application of radium before hysterectomy, 60 per cent were reported as cured.¹⁵ These results indicate that the combined method of treatment is to be advocated, whenever practical, for all patients. It is particularly important in those with undifferentiated tumors. Radiation alone may prove to be the best procedure in such instances. That will be decided after a large number of patients suited to surgery have been observed in clinics treating all cases of corpus cancer by irradiation.

In the radium treatment of corpus lesions it is difficult to determine the size and location of the tumor. The disease may form a bulky mass that will distort the cavity so greatly that radium cannot be applied in a manner that will deliver a suitable distribution of radiation. Approximately 20 per cent of the cases are complicated with myomas that may also distort the cavity. Sampson¹⁸ has demonstrated those difficulties by means of radiographs taken of removed uteri into which had been placed capsules to simulate the radium treatment of corpus cancer. He also discussed the danger of the radium capsule acting as a piston to force blood containing tumor cells through the lumina of the

should be removed before irradiation. In some instances tumors may disappear, or decrease in size so that they can be removed at a later date.

For irradiating ovarian tumors the entire abdomen should be included. It is usually necessary to employ upper and lower abdominal areas on both the anterior and posterior surfaces. The operative scar should be included in the direct beam, due to the frequency of recurrences in that region from implantation metastases. Complete treatment will usually require from two to three weeks. During that time from 1,000 to 1,500 roentgens can be delivered to each area.

CARE OF THE IRRADIATED PATIENT

It is desirable, whenever possible, to keep patients ambulatory and reasonably active during a course of roentgen treatment. The presence of an abdominal dressing does not interfere materially with the administration of external irradiation. However, it is essential that all adhesive tape be removed from the *skin fields*, and that the tape never be replaced to those areas after treatment. This is necessary because the presence of adhesive will in every instance increase the reaction in the underlying skin. Mild irritation of the irradiated fields can be treated with any bland skin lotion. If ulceration occurs, then vaseline or olive oil dressings give greater relief.

Intestinal irritation from x-rays or radium can be diminished usually by regulating the diet, and the use of opiates, etc. The discomfort from severe proctitis may be relieved by injecting several times a day a few cubic centimeters of warm oil, or the insertion of suppositories containing some anesthetic. Mixtures containing tinctures of belladonna and hyoseyamus are useful in the treatment of cystitis. Every patient should receive daily a vaginal douche of some antiseptic solution, such as potassium permanganate (1:1,000).

The amount of radiation required for the treatment of malignant diseases of the reproductive system may produce some anemia and leucopenia. Various medications and sedatives that may have a damaging effect upon blood cells should be avoided.

Patients should be observed at frequent intervals during their convalescence following irradiation. It is essential that all patients with malignant disease be followed carefully by regular and periodic examinations, so that any complication, or recurrence of the disease, will be recognized at the earliest time possible.

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The results have not been satisfactory. It should be noted that the age incidence of vulval cancer is so high that many patients die of intercurrent disease before the five-year period has elapsed.

For the double-sided Basset operation, Taussig²³ reports an operability of 75 per cent, and a primary mortality of only 4.6 per cent. In a series of 23 patients treated by that method he obtained a five-year cure rate of 65 per cent, and among 12 patients 55 per cent survived ten years. Those statistics are probably among the best that have been given for vulval cancer.

Healy¹⁶ states that among 8 patients who survived the five- to ten-year period, surgical removal of the vulva, and dissection of one or both groins was the important procedure in each instance. However, all of the enlarged inguinal glands were not infiltrated by the disease. He feels that dissection of the groins is not essential in every instance. For some time he has omitted radiation in the treatment of the primary lesion, which is removed by complete vulvectomy. The groins are treated with x-rays. If nodes appear in those regions, they are exposed and gold seeds implanted so as to deliver not less than 5 threshold doses.

CARCINOMA OF THE VAGINA

Carcinoma of the vagina has been cured rarely by surgery alone. For radiation Healy¹⁶ reports a five-year cure rate of 12 per cent. In 129 irradiated cases he cited from the literature, 12.4 per cent survived that period. The soft, friable, vascular lesions of the cauliflower variety usually show the greatest response to radiation. Only palliative results can be obtained in the large annular lesions filling the vagina. Fistulas into the bladder or rectum are fairly common sequelae, if the primary lesion is located in the vesicovaginal or rectovaginal septum.

Treatment should be given with both x-rays and radium. A protracted roentgen treatment with multiple exposures totaling 1,500 to 2,000 roentgens to each area will usually produce considerable regression in the size of the lesion. Following this procedure various plaques, or other intravaginal applicators containing radium, can be used at distances of about 1.0 cm. for doses ranging from 1,000 to 2,000 mg. hr. The total amount of radiation delivered to the diseased area can be increased if it is practical to use interstitial sources of radium in addition to the above methods.

OVARIAN TUMORS

Ovarian tumors present a wide variety of histologic types, some of which respond to radiation, while others remain relatively unaffected. A favorable response has been noted rather consistently in those that contain calcium deposits in the form of psammoma bodies. Practically all of the embryonal carcinomas, and other undifferentiated types are radiosensitive. However, biopsy is difficult to obtain, and the variety of tumor in question is not known usually until after operation. In some instances tissue for histologic diagnosis has been obtained by cul-de-sac puncture.

Whenever practical the patients are usually treated surgically. Tumors that prove to be malignant are given postoperative irradiation. Healy¹⁶ states that the five-year cures from surgery vary from 10 to 15 per cent.

If for various reasons the tumor cannot be treated surgically, all large amounts of fluid present in the abdomen or in cysts of the tumor

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Ectopic Pregnancy

Logwinsky, P. N.: Tubal Pregnancies in Our Clinic (Kiew), *Monatschr. f. Geburtsh. u. Gynäk.* 100: 25, 1935.

At the Kiew Clinic were found histories of 129 ectopic pregnancies. Inflammatory changes in the pelvic organs especially in the tubes were noted in most cases and considered to be the cause of the tubal pregnancy in most instances. The largest proportion of cases of ectopic pregnancy occurred in the ampullar portion of the tube. The best treatment for ectopic pregnancy is complete removal of the pregnant tube with excision of the uterine horn. For quick peritonealization of the raw surfaces, the round ligament may be used. Because of the infrequency of the recurrence of ectopic pregnancies and the relatively high incidence of normal conceptions after tubal pregnancies, the author believes that the nonpregnant tube should be left in place. The latter should be removed only if it shows gross abnormalities.

J. P. GREENHILL.

Fulconis, H.: Familial Ectopic Pregnancy, *Bull. Soc. d'obst. et de gynec.* 25: 56, 1936.

The author reports 3 cases of ectopic pregnancy occurring in two sisters and a daughter of one of them. Two of the three women were operated upon within one week. In all three cases the right tube was involved.

J. P. GREENHILL.

Duseberg, G.: Origin and Types of Abdominal Pregnancies, *Monatschr. f. Geburtsh. u. Gynäk.* 102: 30, 1936.

The causes of premature ectopic nidation of ova may be divided into intra- and extraovular causes. The intraovular causes consist of an abnormally large ovum, unusually rapid growth of the ovum and infections or degenerative changes in ova or sperm. The extraovular causes are divided into constitutional and acquired predispositions. Among the inherited tendencies are hypoplasia of the tubes which are therefore long and tortuous and have defective development of the tubal mucosa, anomalies of the ciliated epithelium and hypoplastic musculature. The tubes may be congenitally deformed or entirely missing. The deformities may include accessory tubes, abnormal tubal openings or tubal diverticula in any of which an ovum may become implanted. Another constitutional factor in women over forty years of age is senile involution of the tubes.

The acquired factors responsible for ectopic pregnancies are chiefly deformities of the tubes due to illness, inflammations and treatment. In addition to these malformations intra- or extratubal tumors such as polyps, fibromas, or ovarian tumors

Society Transactions

NEW-YORK OBSTETRICAL SOCIETY

MEETING OF OCTOBER 13, 1936

The following papers were presented:

Extraperitoneal (Latzko) Cesarean Section. Dr. Albert H. Aldridge. (For original article, see page 788.)

The Endocrine Basis of Toxemia of Pregnancy. Drs. J. J. Vorzimer, E. G. Langrock, A. M. Fishberg, and E. M. Rappaport. (For original article, see page 801.)

MEETING OF NOVEMBER 10, 1936

The following paper was presented:

A Study of Dermoid Cysts With a Suggestion as to the Use of X-ray in Diagnosis. Dr. Morris Glass and Dr. Alexander H. Rosenthal. (By invitation.) (For original article, see page 813.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF NOVEMBER 5, 1936

The following papers were presented:

On Certain Pharmacologic Actions of the Newer Barbituric Acid Compounds. Dr. Charles M. Gruber. (For original article, see page 729.)

Analgesia With the Barbituric Acid Derivatives and Its Relationship to Sudden Death in Labor. Dr. Thaddeus L. Montgomery. (For original article, see page 745.)

patency. Here again, however, it is conceivable that inspissation or encapsulation of the oil within or about the tubes may occur and thus defeat the purpose for which it was introduced.

From the experience with the extrauterine pregnancy here reported, the author concludes that the uterotubal injection of iodized oil is not entirely harmless. It appears that the oil is not only slowly absorbed and may, by remaining in the tubes for as long as two years, retard the advent of pregnancy, but such delay in absorption may be also a factor in the development of extrauterine pregnancies. In the case here reported, it is conceivable that the oil became encapsulated at the right fimbriated end, and thus did not permit the impregnated ovum to reach its normal place of nidation within the uterus.

J. THORNWELL WITHERSPOON.

Hoffman, A. I.: Complete Tubal Abortion From Columnar Implantation of the Ovum, Gynec. et obst. 33: 520, 1936.

Upon the site of implantation of the ovum depends the mode of termination of a tubal pregnancy. Most frequently it terminates by tubal abortion, in which case the ovum is usually in the ampullar portion of the tube. If situated in the isthmus tubal rupture occurs.

In complete tubal abortion, which is uncommon, the entire ovum is expelled, and if there is no marked alteration of the tubal musculature the tube contracts with arrest of hemorrhage, and involution follows.

Implantation of the ovum in the ampulla may occur on the summit of a plical fold. Werth termed this "Columnar Implantation" as distinguished from "Inter-columnar Implantation" with implantation between the plicae. In the former the muscle wall remains intact or almost so for five or six weeks, particularly if the ovum succumbs early. The ovum thus suspended in the lumen of the tube by a pedicle consisting of the plica is swept by reverse peristalsis into the abdomen.

Clinically, complete tubal abortion is characterized by delay in menstruation, sudden onset of abdominal pain, and signs of internal hemorrhage and shock. From his personal experience with three patients presenting this condition the author stresses several important operative findings. There is massive peritoneal hemorrhage with the source of bleeding not apparent. The affected tube is markedly hyperemic and the ampullar portion, in contrast to the isthmus, is somewhat dilated. He suggests that the tube be gently compressed between two fingers and milked from the isthmus toward the abdominal ostium; this will express the small black blood clots that remain within the tube after complete expulsion of the ovum.

In reference to treatment he advises salpingectomy for the following reasons: (1) Hemorrhage may recur from site of detachment of ovum; (2) trophoblastic elements which are present in considerable quantity may give rise to hemorrhage as an immediate complication, or to placental mole or chorionepithelioma as a late complication; (3) the affected tube though involuted remains a potential site for another ectopic gestation.

ARNOLD GOLDBERGER.

Paola, Guillermo Di, and Ibanez, Anibal Lemos: Bilateral Simultaneous Tubal Pregnancy, Bol. Soc. de Obst. y ginec. (Buenos Aires) 14: 837, 1936.

The authors present a case of bilateral tubal pregnancy. They state that in the literature they could find only 4 such cases heretofore mentioned.

The theories for such an occurrence are as follows: (1) Fecundation of 2 ova from distinct follicles in the same ovary; (2) Fecundation of 2 ova from different follicles of both ovaries; (3) Fecundation of 2 ova belonging to the same follicle.

The treatment was salpingectomy, bilateral in this case, as both tubes were involved.

MARIO A. CASTALLO.

may compress the tubal lumen or kink tubes and thus interfere with the progress of an ovum. Inflammations may produce changes both inside and outside of the tubes. While gonorrhea is the most frequent type of inflammation leading to ectopic pregnancy, others such as tuberculosis, appendicitis, abortion and puerperal infection may play a rôle.

Part of the increased frequency of tubal pregnancies is due to the increase in therapeutic and prophylactic manipulations such as curettements, the use of intra-cervical pessaries, intrauterine instillations for the purpose of producing abortions, the injection of iodized oil and contraceptive devices.

J. P. GREENHILL.

Morillo, Luis: The Diagnostic and Prognostic Value of the Aschheim-Zondek Reaction in Extrauterine Pregnancy, *Ztschr. f. Geburtsh. u. Gynäk.* 110: 18, 1934.

Morillo gives a brief résumé of 13 cases of extrauterine pregnancy proved by operation. Aschheim-Zondek tests were made in each case prior to operation. In only five cases was Reaction III positive, in only one was Reaction II positive, and in the remaining seven cases Reaction I was positive. There were no complete negative results. According to the literature Reaction III is positive in from 72 to 91 per cent of all extrauterine pregnancies. The author injected animals with extracts of chorionic tissue obtained at operation in several of the cases, and found that positive reactions could be obtained only with relatively large amounts of tissue when the pathology in the pelvis was of long standing. He therefore concludes, agreeing with other writers on the same subject, that the A-Z Reaction III is always positive early in the development of an extrauterine pregnancy, but becomes negative as the chorion loses its function through the death of the ovum. A positive Reaction III indicates that the chorion is still functioning, or that it has functioned within the past few days.

EUGENE S. AUER.

Piraino, Amedeo, and Santomauro, Ugo: Unilateral Pupillary Dilatation as a Diagnostic Sign in Extrauterine Pregnancy, *Folia gynæc.-demograph.* 32: 153, 1935.

In one-third of their cases of extrauterine pregnancy, the authors found a mydriasis of the pupil of the eye on the same side where the extrauterine pregnancy was situated. This sign may be found throughout the course of the pregnancy, and disappears only upon the surgical removal of the pregnancy, and under very deep anesthesia.

The sign although not specific should be watched for, because (1) other causes of unilateral dilatation of the pupil are easily differentiated from pregnancy; (2) the sign is present during the entire period of the extrauterine pregnancy; (3) it is an objective sign; and (4) it is easily and quickly recognized.

MARIO A. CASTALLO.

Polowe, David: Extra-Uterine Pregnancy Following the Injection of Iodized Oil for Uterosalphingography, *Am. J. Surg.* 29: 244, 1935.

Insufflation with gaseous products may successfully establish tubal patency. However, in cases of partial obstruction, such a procedure does not prevent the collapse of the tubes with the consequent reformation of intratubal adhesions as soon as such gases are absorbed (a matter of less than a day when judged by the cessation of shoulder pain). Radiopaque oils, on account of their slower absorption, therefore, may prove more successful than gases in the maintenance of tubal

Since it attracts attention between twelfth and twentieth weeks of gestation, it should be differentiated from ectopic pregnancy, pregnancy in a rudimentary horn, fibromyomas undergoing degeneration, torsion of the pedicle of an ovarian cyst, appendicitis with lateral flexion of the uterus and finally, pyelitis with pregnancy.

F. L. ADAIR AND S. J. BENENSOHN.

Guillemin, A.: Peritoneal Hemorrhage From a Ruptured Ovarian Follicle, Soc. d'obst. et gynec. 25: 497, 1936.

A young girl was operated upon because of a severe intraabdominal hemorrhage as a result of rupture of a corpus luteum. The author removed the involved ovary. This operation was performed March 21, 1935, when the patient was sixteen years old. On Jan. 26, 1936, she had a second laparotomy for a similar condition on the opposite side. The second ovary was removed but the author transplanted a portion of it under the skin. The first hemorrhage resulted four days before the expected menstrual period, while the second one appeared fifteen days after the last menstrual period.

J. P. GREENHILL.

Tomasi, Luigi: Primary Abdominal Pregnancy, Clin. obst. (Bari) 37: 404, 1935.

The author describes a case in which the physical examination revealed all the classical symptoms of a ruptured tubal pregnancy, while during laparotomy the uterus and fallopian tubes were found to be normal. The source of the imposing hemorrhage was a hemorrhagic tumor situated on the anterior surface of the rectum.

He maintains that this was a case of true primary abdominal pregnancy.

AUGUST F. DARO.

Costa, Nicanor Palacios, and Falsia, Antonio: Ovarian Pregnancy, Bol. Soc. de obst. y gynec. (Buenos Aires) 14: 126, 1936.

A patient with an ovarian pregnancy is reported. The preoperative diagnosis was ectopic pregnancy. Histologic slides are shown to prove the correctness of the diagnosis.

MARIO A. CASTALLO.

Fox, E. A.: Extrauterine Pregnancy Partially Eliminated Through the Intestinal Tract, Bol. Soc. de obst. y gynec. (Buenos Aires) 14: 121, 1935.

The author reports the history of a forty-one-year-old multipara with undiagnosed abdominal pathology on admission to the hospital. During observation period the patient passed a fetal tibia and clavicle while defecating.

Roentgenography disclosed a fetal skull in the pelvis, which was found to be in the large intestine at operation for its removal through the abdominal route. Uneventful recovery.

MARIO A. CASTALLO.

Hosking, Archer: Abdominal Delivery of 254-Day Extrauterine Foetus, Brit. M. J. 2: 111, 1934.

The author describes the removal of a fetus from the abdomen by laparotomy at 254 days. The operation was exceedingly simple. The placenta had remained completely within the tube, and the absence of adhesions was remarkably favorable.

The patient, aged 35, had had an ectopic pregnancy three years previously at seven weeks' pregnancy, followed by removal of the right tube. No other preg-

Nandi, G. C.: Simultaneous Intra-Uterine and Extra-Uterine Pregnancy, Calcutta M. J. 29: 159, 1934.

A case of simultaneous intra- and extrauterine pregnancy is reported. Para ii, aged twenty-five, last child fourteen years ago. Past history negative.

Last menstrual period occurred end of May, 1933. Acute pain in lower abdomen and bloody vaginal discharge started middle of July. She entered hospital, Sept. 3, 1933, complaining of pain in lower abdomen and constipation. Findings: Soft mass 2 fingers below umbilicus, toward the right side, not freely movable. Cervix soft and bulky, uterus anteverted and pushed forward by a mass attached to the uterus.

Abdominal section revealed dark blood in peritoneal cavity, a pelvic hematoma behind uterus and to left, intimately connected with corpus. Uterus was size of eight weeks' pregnancy. Left tube and ovary adherent to mass. Right appendages normal. Chorionic villi in mass and rent in left tube visible. On section uterus found to contain a fetus of eight weeks. Patient made uneventful recovery after removal of uterus and appendages.

This condition has been termed "simultaneous pregnancy," "combined pregnancy," or "compound pregnancy." It is rare since only 217 cases have been found in the literature by Gemmel and Murrey in 1933. It may be a type of twin pregnancy, one fertilized ovum implanting itself in uterus, the other in the tube; in other cases, the condition may be due to the superimposition of a uterine pregnancy upon one already existing in the tube. The latter may antedate the uterine gestation by a long or very short interval.

The literature is reviewed.

F. L. ADAIR AND S. A. PEARL.

Kerr, J. M., and Anderson, D. F.: Angular Pregnancy. A Clinical Entity, Brit. M. J. 1: 1113, 1934.

Author gives histories of two cases of cornual pregnancy seen in the Glasgow Royal Maternity and Women's Hospital.

Case 1, a gravida vi, fifteen weeks pregnant. Because of acute abdominal symptoms a laparotomy was performed with a provisional diagnosis of ectopic pregnancy or torsion of ovarian cyst. Exploration revealed marked elongation of the right cornu and abdomen was closed. Patient developed a pneumonia and aborted spontaneously the day following laparotomy.

Case 2, a primigravida, aged twenty-one, who before admission complained of acute abdominal cramplike pains, tenderness in right lower quadrant, tender and hard uterus. On bimanual examination a tender elongated right cornu was palpated and a diagnosis of nineteen-week angular pregnancy was made. Throughout the pregnancy she experienced these sharp pains. At thirty-five weeks gestation uterus was lying to the right side and was tender. Patient had a forceps delivery of a 5 pound 10 ounce child and uterus was explored; placenta was attached in the elongated right cornu.

Kerr discusses angular pregnancy as a particular type of gestation in which the zygote becomes implanted in one horn of the uterus and thus is distinct from the interstitial variety of ectopic. He states that he had previously observed four such cases and all six were similar in the following features: (1) Pain, (2) lateral distention of the uterus in the region of the uterine cornu, (3) tendency to abortion. Three of six cases ended in abortion.

Books Received

INTIMATE SIDE OF A WOMAN'S LIFE. By Leona W. Chalmers. Illustrated, 128 pages. Pioneer Publications, Inc., Radio City, N. Y., 1937.

PHYSICIANS' GUIDE BOOK for Mothers. By G. G. Keener, M.D. Southern Publishers, Inc., Kingsport, Tenn., 1936.

SAFE CHILDBIRTH. The Three Essentials. By Kathleen Olga Vaughan, formerly medical officer, Egyptian Quarantine, etc. With foreword by Howard A. Kelly. Illustrated, 154 pages. William Wood and Company, Baltimore, 1937.

DISEASES OF INFANTS AND CHILDREN. By J. P. Crozer Griffith, M.D., Emeritus Professor of Pediatrics in the University of Pennsylvania, etc., and A. Graeme Mitchell, M.D., Professor of Pediatrics, College of Medicine, University of Cincinnati, etc. Second edition, revised and reset. Illustrated, 1154 pages. W. B. Saunders Company, Philadelphia, 1937.

PREOPERATIVE AND POSTOPERATIVE TREATMENT. By Robert L. Mason, M. D., assistant in surgery of the Massachusetts General Hospital. Illustrated, 495 pages. W. B. Saunders Company, Philadelphia, 1937.

KAMA SUTRA, the Hindu Science of Love. Translated from the Sanscrit by Sir Richard Burton. Illustrated, 127 pages. The Medical Press of New York, New York, 1936.

DAS HORMON DES CORPUS LUTEUM. Von Dr. Erich Fels, Instituto de Maternidad de la Sociedad de Beneficencia, Buenos Aires. Mit 40 Abbildungen im Text, 169 Seiten. Franz Deuticke, Wien, 1937.

Item

American Board of Obstetrics and Gynecology

Practical oral-clinical, and pathological examinations for Group A and Group B applicants will be held at Atlantic City, N. J., on June 7 and 8, 1937.

An informal dinner for the Diplomates of this Board and others interested in obstetrics and gynecology will be held at the Hotel Claridge, Atlantic City, on Wednesday, June 9, 1937, at 7:00 P.M. At this time several short addresses will be made and the successful candidates of the preceding two days' examinations will be introduced in person.

Applications for the Group A examination will be received in the office of the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa., to April 9, 1937. Application blanks may be secured from the Secretary's office.

nancies occurred until the present. Constipation and lower abdominal pain were present throughout pregnancy.

The baby weighing 5 pounds 12 ounces survived nine hours. The mother recovered after a complicated puerperium of seven weeks. Normal menstruation was established three months after operation.

F. L. ADAIR AND S. A. PEARL.

Krishnan, R. G.: Full-Term Extrauterine Pregnancy: Child Delivered Alive, Brit. M. J. 1: 795, 1936.

The record is given of a full-term extrauterine pregnancy in a para vii, aged thirty-three, delivered of a live child by laparotomy. The placenta lodged in the layers of the left broad ligament and the amniotic cavity was firmly enclosed by adhesions. The uterus appeared to be the size of a twelve weeks' gestation. Pain during pregnancy and slight periodic vaginal bleeding occurred. Recovery was uneventful.

F. L. ADAIR AND S. A. PEARL.

Steel, W. Arklay: Full-Term Extrauterine Pregnancy With Living Child, Brit. M. J. 2: 62, 1934.

Primipara, aged twenty-four, with a ventral hernia due to an appendicitis operation scar. Complained of very severe "knifelike" pains. Temperature, pulse, and urine were normal. There was marked tenderness over the entire abdomen. The cervix was soft and the external os closed. The fetus was found lying transverse. An external version was attempted, when a "snap" was felt and then a large placenta made out, occupying the entire pelvis. The patient became shocked. The uterus was thought to be ruptured and a laparotomy done. A living female child was extracted from the abdominal cavity which was filled with blood. The uterus was anterior to the placenta. The placenta was attached by a broad pedicle (3 to 4 inches) to the posterior aspect of the right broad ligament. A pint of blood sucked out of the peritoneal cavity was given to her intravenously. She rapidly improved, showing the value of auto-transfusion. The child seemed healthy but died suddenly twelve hours after birth. Autopsy on the child showed nothing abnormal.

F. L. ADAIR AND I. BROWN.

Tallaferro, Federico: A Case of Extrauterine Pregnancy at Term, Bol. Soc. de obst. y ginec. (Buenos Aires) 15: 411, 1936.

The author reports a case of extrauterine pregnancy at term. The case was diagnosed by x-ray after injection into the uterus of a radiopaque substance. A live child was obtained by means of abdominal operation. Most of the placenta was left in situ, with drainage through Douglas' pouch. The patient finally died from peritonitis.

MARIO A. CASTALLO.



Robert J. Frank

cepted and much-quoted standard. Studies dealing with the problem of uterine prolapse and its treatment, as well as that of vesicovaginal fistula, and of other plastic procedures, including the construction of an artificial vagina, constitute noteworthy additions to American gynecologic literature.

The assembled contributions to this volume represent the work of many collaborators from various American and foreign sources. Their dedication for this purpose is not merely a flattering compliment to Dr. Frank, it is an acknowledgment of that widespread and well-established interest in the diseases of woman peculiar to her sex and in the care of her reproductive processes.

The last century has been replete with great advances in the combined field of obstetrics and gynecology. The acceptance of the contagious character of puerperal fever, the establishment of the principles of antisepsis and asepsis, the clinical application of anesthesia, the extension of operative methods of approach in pelvic disease and in the dystocia of labor almost seemed to spell the end of progress at the turn of the century. But much remained in reserve for further development during the next three decades when radiation procedures for diagnosis and treatment, blood transfusions for postoperative hemorrhage, adequate and prophylactic prenatal care methods, a better understanding of the physiology and histology of menstruation and its abnormalities, and an increasing insight into the mysterious workings of the endocrine glands, constituted an era of progress which opened up new worlds of thought and activity. It is during this latter period that Robert Frank has made his noteworthy contributions in the field of endocrinology, noteworthy because they were based on careful clinical observations, supported by animal and pharmacologic experiments. The additions to our knowledge of the activities of the endocrines made by Dr. Frank and his coworkers constitute an outstanding contribution to American medical literature and represent that sane application of theoretic knowledge to clinical procedures which is often lacking but is so very important and essential.

The Editors of the JOURNAL are happy to have been afforded the opportunity to present to the medical profession these assembled contributions from outstanding clinicians and research workers, dedicated to a man who, by earnest effort and continued application, has contributed much to our knowledge in a special field of medicine. This volume and what it represents, will undoubtedly constitute a source of gratitude and satisfaction to its recipient, conveying as it does, a united expression of good will and good feeling from its numerous contributors to Dr. Frank upon his retirement merely from active service in the Mount Sinai Hospital, which he long has served so ably and so well.

—George W. Kosmak, M.D.

American Journal of Obstetrics and Gynecology

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Robert T. Frank Anniversary Number

ROBERT TILDEN FRANK

AN APPRECIATION

THE present issue of the JOURNAL possibly is an innovation in that it constitutes a memorial to a man still active in his chosen profession, who has before him a span of years when he may enjoy the fruits of his labors and the honors which have been bestowed upon him. In this country we do not always acknowledge a man's achievements during his lifetime nor do we afford an opportunity for his friends and colleagues to do so in a cooperative manner such as is afforded in this special issue of the JOURNAL. The Germans have a word for it, they call a volume like this a "Festschrift"—unfortunately we have no equivalent term. But its meaning and scope are clear, let us call it what we may.

This volume, as put forth, commemorates a man's career, a career which is synchronous with great advances in gynecology, advances which have altered the conception of this important branch of medicine from its previously mechanistic character to one much broader and more significant. It also presents a compliment of universal appreciation of the influence which Dr. Frank has wielded in molding present-day thought and opinion, especially in that twilight zone of endocrinology and its allied histology and pathology, in which much has been accomplished but in which much still remains to be done.

But Dr. Frank's scientific activities have not been limited to the domain of endocrinology. His work on gynecologic and obstetric pathology, first published in 1931 and since then twice revised, is an ac-

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

Fig. 1.—Cross-section of the ampulla of the fallopian tube of the sow showing the injected lymphatics (from Andersen¹). The most conspicuous lymph plexus is situated in the mucosa. The vessels in this plexus are typical lymph capillaries without valves. Those in the mucosal folds empty into similar vessels at the base of the folds. Vessels from the latter pierce the inner muscular layer and empty into valved collecting vessels situated between the two muscular layers. These vessels in turn empty into lymph vessels in the mesosalpinx. The subserous plexus is less conspicuous and consists of small capillaries just outside the outer muscular layer, separated from the serosal mesothelium by a few strands of connective tissue. This plexus also drains into the intermuscular vessels. $\times 56$.

Fig. 2.—Photomicrograph of a portion of an oblique section of the ampulla of a normal appearing tube. The patient, A. H. No. 1920-22, parous, aged forty-one, had had the entire uterus and one tube and ovary removed for a primary uterine endometriosis. Irregular-shaped channels or spaces lined by endothelium-like cells are present in some of the folds and also at the base of the folds. The form and situation of these spaces are similar to those of the injected lymphatics of the mucosa shown in the preceding illustration. I believe they are lymph vessels. Compare also with the next photomicrograph. $\times 25$.

Fig. 3.—Cross-section of a portion of the ampulla of the left tube in which the lymphatics of a large mucosal fold are filled, as with an injection mass, with carcinoma secondary to that in the ovaries. The patient, A. H. No. 9895, parous, aged forty-seven, had had both tubes and ovaries and the uterus removed for bilateral ovarian carcinoma associated with an extensive peritoneal carcinomatosis. Carcinoma was found in lymphatics in all layers of this tube and also in lymph vessels in the mesosalpinx. The form and situation of the carcinoma-filled lymph vessels in this fold and also in the mucosa at the base of the fold ("a") are very similar to the injected lymph vessels shown in Fig. 1 and also to the judged lymph vessels shown in Fig. 2. The condition present in this section gives added support to the belief that the empty spaces shown in the mucosa of Fig. 2 are lymph vessels. $\times 25$.

review of the lymphatics in the tubal mucosa, Andersen mentions the observations of Henle (1873), Orthmann (1887), Sobotta (1903), Hörmann (1908), Grosser (1919), and Graf Spee (1924). She also states: "A number of workers on the lymphatics of the uterus have likewise discovered the presence of lymphatics in the tube."

Hörmann³ (1908) evidently observed lymph vessels in the mucosa of the fimbriae as well as in the mucosa of the ampulla of the tube. He frequently found large irregular empty spaces in the large mucosal folds of the ampulla and of the fimbriae which he stated had attracted the attention of earlier writers. Hörmann in his paper gave Henle's and Orthmann's descriptions of these spaces. He was first inclined to regard these spaces as artefacts but, after observing that they occurred with great regularity both in form and distribution in all of his preparations and that in many places they appeared to be lined by endothelium, he concluded that although definite proof was lacking, these spaces were most likely lymphatics.

Andersen¹ writes that she has been "able to discover in an earnest perusal of the literature . . . no description whatsoever of the pattern of the lymph vessels within the tubal wall." The absence in the literature of a description of the intrinsic lymphatics of the tube is due to the difficulties encountered in injecting these vessels.

Andersen¹ injected the lymphatics of the tubes of sows. She was able to obtain injections of the lymphatics of all portions of the ampulla of the tube and of the tubouterine junction in that animal. Due to technical difficulties she was unable to inject the lymphatics of the mucosa of the isthmus of the tube and of the infundibulum. She believed, however, that the infundibulum does contain a lymph capillary plexus as yet not demonstrated.

THE LYMPHATICS OF THE MUCOSA OF THE FIMBRIAE OF THE FALLOPIAN TUBE

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(From the Gynecological and Pathological Departments of the Albany Hospital and the Albany Medical College)

IT IS the purpose of this paper to present observations made in the endeavor to ascertain the distribution of the lymph vessels in the mucosa of the fimbriae of the fallopian tube and their relation to the lymphatics of the ampulla of the tube and to those of the mesosalpinx and the ovary.

In the study of carcinoma of the tubal mucosa secondary to carcinoma of the ovary, I have been impressed both with the frequency of the location of these secondary tumors in the fimbriae of the tube and also, in some of these cases, with the presence of the growth in spaces which I believed might be lymph vessels of the mucosa of the fimbriae. In attempting to determine the pathogenesis of these secondary tumors I have been handicapped by a lack of any conception not only of the distribution of the lymphatics in the mucosa of the tubal fimbriae but also of their relation to the lymphatics of the ampulla of the tube and those of the mesosalpinx and the ovary.

Andersen¹ (1927) referred to the contributions of Poirier (1889-90), Bruhns (1898), Bartels (1909), and Poirier and Cuneo (1920) indicating that the lymph vessels from the tube empty into the subovarian plexus and there unite with lymph vessels from the ovary and the uterus. Andersen has shown that in the sow (Fig. 1 of her paper) the lymph vessels from all portions of the tube, including the fimbriae, converge to form the subovarian plexus which also receives lymph vessels from the ovary and the uterus.

Pellé and Pellé² (1931) by first injecting the lymphatics of the tubes with Paris blue and then those of the ovary or uterus with yellow of cadmium observed that the blue-colored lymph vessels, coming from the tubes, soon became green, thus indicating an early communication between the lymph vessels of the tube and those of the ovary and the uterus. They believe that their experiments verify the opinions expressed by Bruhns and by Bartels to which they refer in their paper. These anatomic observations may be further confirmed by the abundant evidence that carcinoma may spread from either the uterus or the ovary to the tube by way of the lymph vessels.

Little apparently is known about the lymphatics in the tubes of women and least of all about those in the fimbriae.

Andersen¹ states: "The existence of lymphatics in the fallopian tube has been suspected for a long time by the students of the histology of the tube. They have noted only the lymphatics of the mucosal folds of the ampulla." In a historical

Fig. 4.—Cross-section of a portion of the ampulla of the left tube in which the lymphatics are filled, as with an injection mass, with carcinoma secondary to that of the ovary. The patient, A. H. No. 93646, nulliparous, aged forty-six, had had both tubes and ovaries and the uterus removed for a large carcinoma of the left ovary. No evidence of peritoneal carcinomatosis was observed at the operation. Compare with Figs. 1, 2, and 3. The distribution of the lymph vessels of the mucosa both in the folds and at their bases is similar in all four illustrations. By noting the lymphatics in each mucosal fold of this section and superimposing the folds on each other one can visualize the distribution of the lymphatics as seen in cross-sections of these mucosal folds. $\times 54$.

Fig. 5.—Cross-section of the ampulla of the tube in which lymphatics in all layers of the tube are filled, as with an injection mass, with carcinoma secondary to that of the uterus. The patient, A. H. No. 4727-31, parous, aged sixty-four, was operated upon for uncontrollable bleeding due to an advanced carcinoma of the uterine cervix which had been treated with radium. An attempt was made to ligate the blood supply of the uterus. The retroperitoneal tissues on both sides of the pelvis were so infiltrated by the growth that it was impossible to gain access to the anterior branch of either internal iliac artery. The right tube and ovary were removed and the left ovarian vessels and both round ligaments were ligated. The bleeding ceased and did not return. The patient died a year later. The study of the tube and ovary removed at operation indicated that the carcinoma had extended from the uterine cornu into the lymph vessels of the mesosalpinx and thence to the ovary and tube. In this section the mucosal lymphatics greatly distended with carcinoma are most striking. Compare with the subserosal lymph vessels which are few in number if their injection is complete. Lymph vessels in the tubal wall are also filled with carcinoma. The carcinoma-filled vessel marked "a" is a collecting lymph vessel extending from the tube into the mesosalpinx at the right. $\times 16$.

The human fimbrial mucosa consists of a continuation of the mucosa of the ampulla with its longitudinal folds through and beyond the abdominal ostium of the tube. This mucosa spreads out and lines the inner surface of the infundibulum of the tube, adapting itself to the size and shape of the latter. It also extends over the rim of the infundibulum and covers the outer surface of the latter for a varying distance to join the serosa of the tube. A further extension of this mucosa along the free margin of the mesosalpinx, toward or to the tubal pole of the ovary, constitutes the mucosa of the ovarian fimbriae.

By floating out the fimbriae of a freshly removed tube in water and by examining it with a hand lens one will be impressed not only with the great variation in the size and shape of the mucosal folds but also with the complexity of their arrangement. If a similar examination is made of the same tube after incising it longitudinally one may see that the arrangement of the fimbrial folds becomes less complex and that the continuity of many of these folds with the longitudinal folds of the ampulla is evident. A comparative examination of several fimbriae demonstrates a great variation in the pattern of the mucosal folds in the different fimbriae. Since the histologic structure of the fimbrial and ampullar mucosa is essentially the same one might infer that the distribution of the lymphatics in the two situations would be similar. A knowledge of the distribution of the lymphatics in the mucosa of the distal portion of the ampulla would be of great assistance in the study of the unknown distribution of the lymphatics in the fimbrial mucosa.



Fig. 1.



Fig. 2.

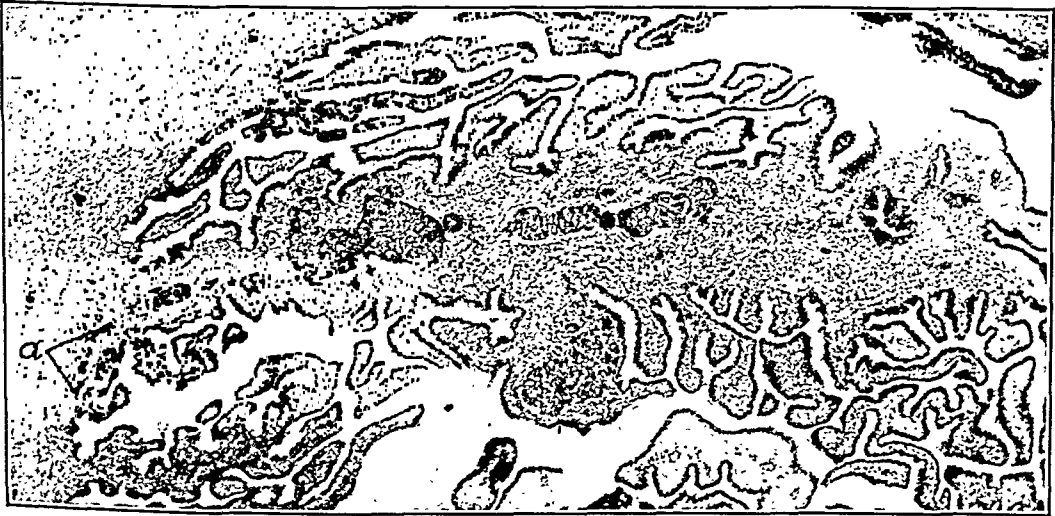


Fig. 3.

Fig. 6.—Longitudinal section of the distal portion of the tube, shown in the preceding illustration, including the fimbriae proper and the free margin of the mesosalpinx with its ovarian fimbriae, at the right, cut obliquely. As in the preceding section, the lymphatics of the mucosa are distended with carcinoma. Many of these are cut either longitudinally or obliquely and are thus extending lengthwise in the tubal mucosa. Note that the fimbrial mucosa is continuous with the mucosa of the ampulla and also that the lymphatics in the mucosa in the two situations appear to be continuous. Large lymph vessels distended with carcinoma are present in the wall of the tube and also in the mesosalpinx beneath the ovarian fimbriae. Apparently the lymph vessels of the ovarian fimbriae drain into vessels in the mesosalpinx beneath. $\times 5$.

Fig. 7.—Higher magnification of a portion of the fimbriae shown in the preceding illustration. The distribution of the lymph vessels in the mucosal folds and at their bases is similar to that shown in the mucosa of the ampulla of this and other tubes (compare with Figs. 1, 2, 3, 4, and 5). $\times 25$.

I have used Andersen's¹ excellent description of the injected lymphatics of the ampulla of the sow's tube as a guide in the study of the lymphatics of the mucosa of the ampulla of human tubes.

"The lymphatics of the ampulla lie in three separate strata of tissue. The two capillary networks lie in the subserous and subepithelial connective tissue respectively, and the large collecting vessels lie in the intermuscular connective-tissue layer. . . .

"In cross-section the most conspicuous plexus is the mucosal one (Fig. 1 of the present paper). The vessels are broad in the long axis of the tube and thin in the transverse axis. They enter each mucosal fold, running approximately perpendicular to the inner surface of the circular muscle, so that if a cross-section cuts through a vessel near the base of the fold it is likely to cut lengthwise through a considerable portion of it. As the lymph-vessel extends farther it divides into two approximately equal branches, usually at an angle of 60 degrees or over, and repeats this method of branching at fairly regular intervals as it continues into the fold. These branches run in all directions through the mucosal folds, but the majority of them run longitudinally with the tube. . . . The vessels are typical lymph capillaries, without valves and with the great irregularity of lymph vessels. . . .

"The lymphatic network of one mucosal fold is connected with that of the next by direct continuity at the base of the folds. This network bears the same relation to the epithelium between folds as to that of the folds proper. At the base of each fold the lymph-vessels widen into small sinuses as they receive the vessels from either side. Similar smaller sinuses are often found at the base of secondary folds. The plexus of vessels in the mucosa thus consists of a rich network just beneath the circular muscle, which receives lymph from the plexus in the mucosal folds. It drains into the intermuscular collecting vessels by way of fairly frequent vessels which pierce the circular muscle, usually in company with arterioles (Fig. 1 of the present paper).

"The lymph-vessels lie in the connective tissue of the mucosal fold. They are separated from the nearest epithelial cells by only a few strands of connective tissue, while they may be a considerable distance, often as much as 50 microns, from other epithelial cells. . . .

"The subserous plexus is less rich, and consists of small capillaries just outside the longitudinal muscle-layer and separated from the serous mesothelium by a few strands of connective tissue. This plexus also drains into large intermuscular vessels. . . .



Fig. 4.

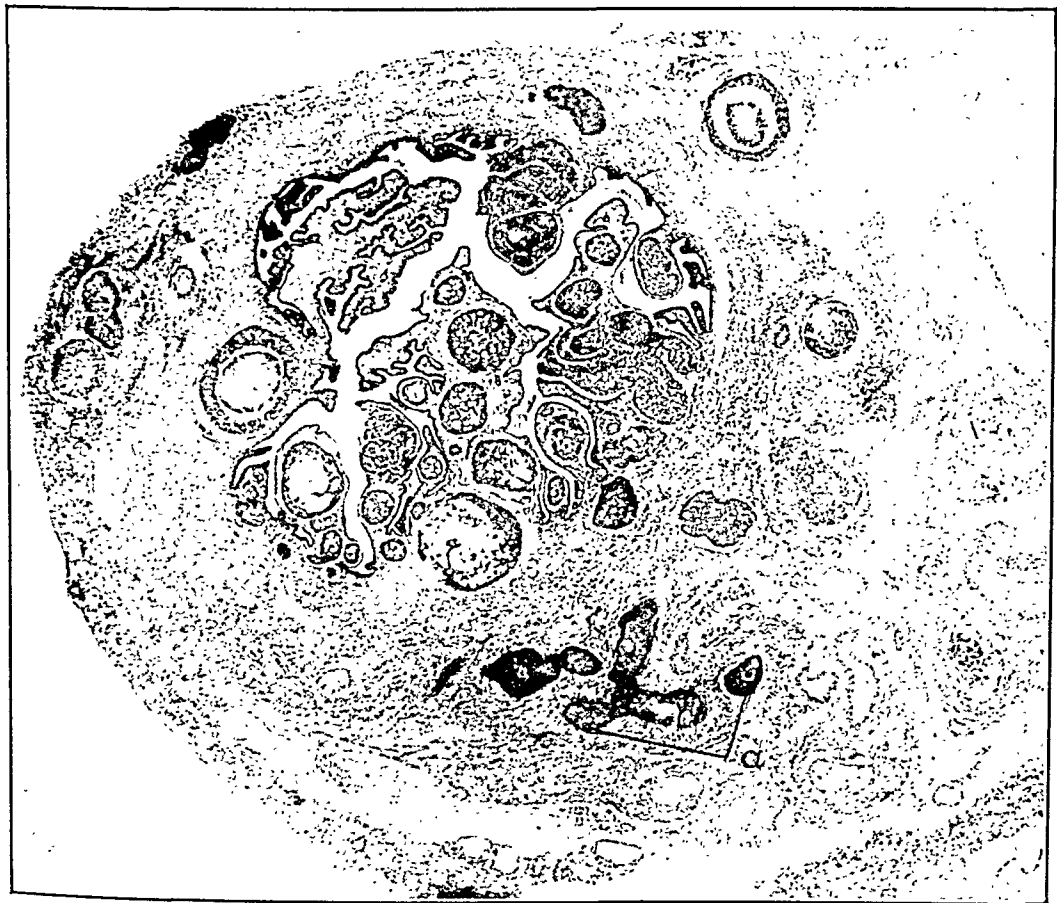


Fig. 5.

Fig. 8.—Longitudinal section of the distal portion of the tube including its fimbriae proper, the mesosalpinx with its ovarian fimbriae and the tubal pole of the ovary at the right. The patient, A. H. No. 9339-31, parous, aged forty-seven, had had the entire uterus and one tube and ovary removed for a uterine leiomyoma. The veins filled with blood appear black in the photomicrograph. Their distribution suggests an intimate relationship between venous outlets of the tubal pole of the ovary, the fimbriae, and the mucosa of the distal portion of the tube. The large irregular empty space "a" arose from an incomplete section of the mesosalpinx. I believe that spaces "b," "c," and "d" are the lumina of large lymph vessels. There is no suggestion of an anastomosis between the lymphatics of the ovarian fimbriae and those of the ovary. Occasional lymph vessels can be seen, under higher magnification, in the compressed folds of the mucosa of the ampulla. On the other hand, dilated lymphatics can be easily seen in many of the folds of the fimbrial mucosa, especially in the folds at the left of the abdominal ostium of the tube. It is obvious even with this low magnification that the fimbrial mucosa is but a continuation of the mucosa of the ampulla beyond the ostium of the tube. $\times 5$.

Fig. 9.—Higher magnification of the fimbrial mucosa about the abdominal ostium of the tube shown in the preceding photomicrograph. The extension of the longitudinal folds of the mucosa of the ampulla through and beyond the ostium of the tube can be easily seen, especially at the left. Lymph vessels running longitudinally in these folds can also be detected. These vessels become more dilated and are therefore more evident the further the mucosal folds extend beyond the ostium. The distribution of the lymph vessels in the folds of the fimbrial mucosa and at their bases is similar to that of the lymph vessels of the mucosal folds of the ampulla shown in this photomicrograph and better pictured in Figs. 1, 2, 3, and 4. $\times 25$.

"The collecting vessels, which are valved, run in the connective tissue which lies between the two muscle-layers." These vessels pass through the tubal wall and empty into the lymph vessels of the mesosalpinx.

METHODS OF STUDY

Although I have failed in all of the few attempts made to inject the lymphatics of the tube, I have, however, observed, in the mucosa of the ampulla of tubes from patients with carcinoma of either the ovary or the uterus, spaces which were filled with carcinoma as with an injection mass. I inferred that these carcinoma-filled spaces were lymphatics. I have also frequently seen irregular, empty spaces in other portions of the tubal mucosa just described and also in the mucosa of normal tubes which, in form and situation, resembled the spaces filled with carcinoma. In these empty spaces an endothelium-like lining could be detected. I gathered this material together and compared the spaces just described with Andersen's¹ illustration and description of the injected lymphatics of the mucosa of the ampulla of the sow's tube. I found that the judged lymphatics observed by me were very similar, both in form and distribution, to the injected lymphatics shown by Andersen (see Figs. 1 to 6). It would seem that Andersen's description of the lymphatics of the mucosa of the ampulla of the sow's tube might at least in a general way be applied to the lymphatics of the mucosa of the ampulla of the human tube.

Realizing that the mucosa of the fimbriae is a continuation of the mucosa of the ampulla through the abdominal ostium of the tube and



Fig. 6.



Fig. 7.

Fig. 10.—Longitudinal section of the distal portion of the tube including the fimbriae, in a plane at right angles to that shown in Fig. 8. The patient, A. H. No. 7788-31, parous, aged thirty-nine, had had the entire uterus and one tube and ovary removed and the pelvic floor repaired for descensus of the uterus and other results of the injuries of childbirth. The veins filled with blood are easily discernible. The lymph vessels cannot be detected in the compressed folds of the mucosa of the ampulla. On the other hand, they are evident in many of the mucosal folds of the fimbriae. A mucoserosal junction is indicated by the letter "a." $\times 10$.

Fig. 11.—Higher magnification of mucosal folds of the fimbriae shown in the lower right-hand portion of the preceding photomicrograph. The lymph vessels in the folds and at their bases can be easily seen. The distribution of these vessels and the ones in the folds of the ampulla, shown in Figs. 1, 2, and 3, is similar. Although lymph vessels for the most part lie in the central portion of the folds, their distance from the epithelium varies in different portions of the folds. Lymph vessels "a," "b," and "c" accompanying blood vessels can be seen in the wall of the tube. If these vessels are continuous with those at the base of the folds, as well they may be, they would furnish an outlet for the lymph in the mucosal lymphatics. $\times 54$.

Fig. 12.—Higher magnification of mucosal folds of the fimbriae at the right of the ostium of the tube shown in Fig. 8. The lymph vessels in the folds and at their bases can be easily seen. The distribution of these vessels and the ones in the preceding photomicrograph is similar. In both instances the tubes were cut longitudinally but in planes at right angles to each other. Note that the blood vessels in the folds are situated, for the most part, between the lymph vessels and the epithelium. This apparently is a consistent arrangement. $\times 25$.

that the mucosa in the two situations has the same histologic structure and therefore should have a similar lymphatic distribution, I studied carcinoma-filled and empty lymphatics of the fimbrial mucosa by comparing them with similar lymphatics in the mucosa of the ampulla.

In order to trace the extension of the mucosa of the ampulla of the tube into the fimbriae fifty-nine normal appearing tubes were studied. The tubes and ovaries attached to uteri which had been removed at operation were severed from these uteri and immediately placed in 10 per cent formalin without incising the tubes. The distal portion of these tubes, including their fimbriae, was imbedded in celloidin since this causes less unequal tissue shrinkage and therefore fewer artifacts than paraffin. The sections were stained with hematoxylin and eosin.

Sections cut in three different planes were employed in the study of these fifty-nine specimens. In one series the distal portion of the ampulla including its fimbriae, the mesosalpinx with its ovarian fimbriae and a small portion of the tubal pole of the ovary were so mounted that longitudinal sections would include all of these structures. In the second series the distal portion of the tube and its fimbriae were cut longitudinally in planes at right angles to those of the first series. In the third series cross-sections were made of the fimbriae and distal portion of the tube. Serial sections were not employed in this group of specimens. However, representative sections from different levels of each block were saved. Lymph vessels could be seen in the mucosa of the fimbriae in all of the sections.



Fig. 8.

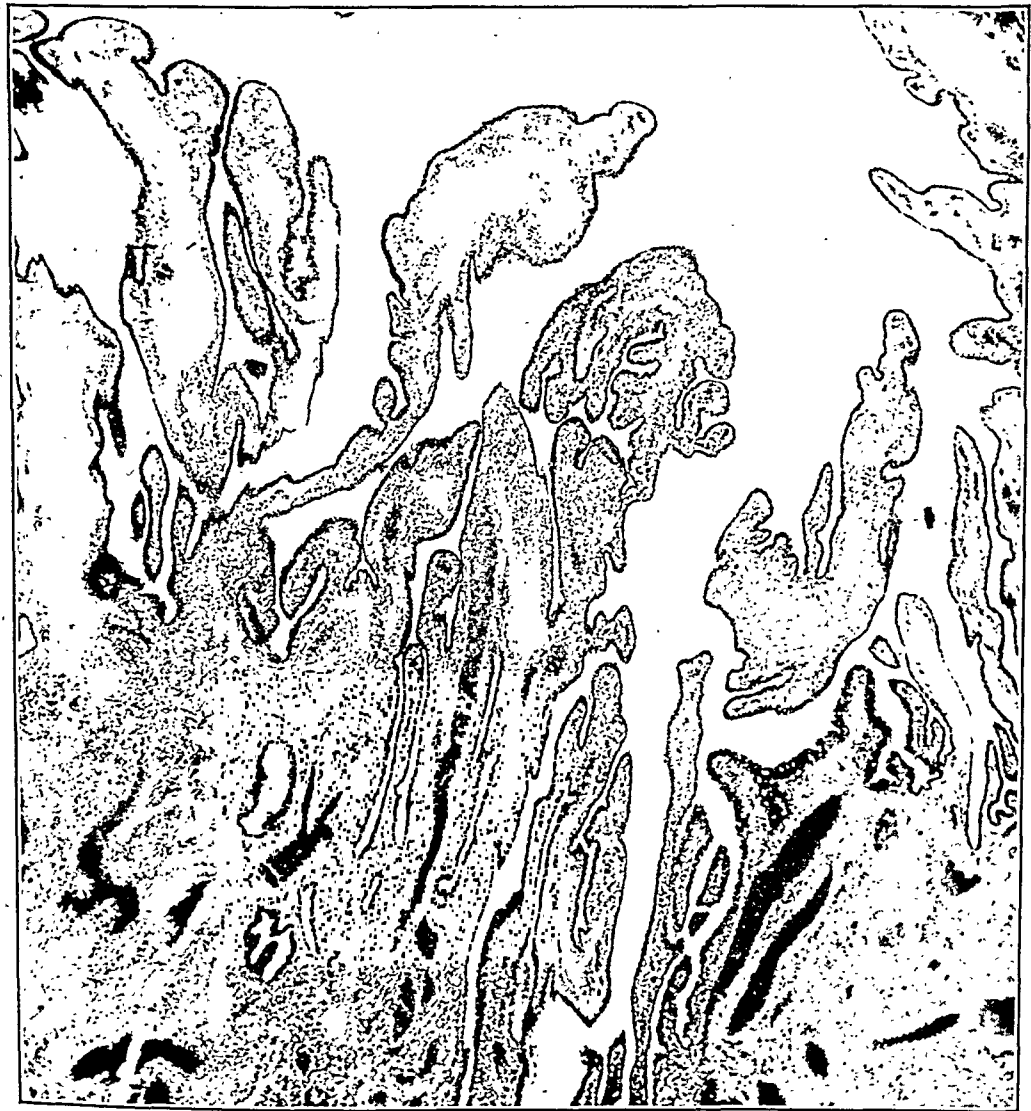


Fig. 9.

Fig. 13.—Mucosal folds of the fimbriae and a portion of the ampulla at the left of the ostium of the tube shown in Fig. 10, from another section. A portion of the ostium of the tube appears at the right in this photomicrograph. Note that the lymph vessels of the folds empty into vessels at the base of the folds. The latter apparently are continuous with lymph vessels of the mucosa of the ampulla and also possibly with lymph vessels "a" and "b" (more evident in lymph vessel "b") beneath the fimbrial mucosa. $\times 54$.

Fig. 14.—Mucosal folds of the fimbriae and a portion of the ampulla at the right of the ostium of the tube shown in the preceding photomicrograph, from the same section. A portion of the ostium of the tube appears at the left in this photomicrograph. Note the lymph vessels in the folds and at the base of the folds. The vessel in the fold nearest the ostium apparently is continuous with the lymphatics of the mucosa of the ampulla. A mucoserosal junction appears in this photomicrograph at "a." There is no evidence of any anastomosis between the mucosal and the subserosal lymphatics. The latter are not evident. $\times 50$.

In a smaller group of five specimens the tubes were incised longitudinally before placing them in formalin. This was done in order that the mucosa of the ampulla would not be compressed by the shrinkage of the wall of the tube in the fixing solution as occurred in the first group. Sections from this group showed no compression of the mucosa of the ampulla with a resulting increased visibility of its lymph vessels. Complete serial sections were employed in a portion of the blocks in all of these specimens. I have found that it is possible to follow a noninjected lymph vessel for only a short distance even in complete serial sections because portions of the vessel may be constricted and therefore difficult or impossible to detect.

The lymphatics seen in the various types of mucosal folds were compared with those seen in similar types of mucosal folds in the same and other sections. In this way one obtained a general impression of the distribution of the lymphatics in each type of mucosal fold.

Noninjected lymph vessels may be confused with empty veins and also with spaces caused by unequal tissue shrinkage. Fortunately the veins in my preparations usually contain blood. Artifacts are infrequent and are usually easily recognized both by their appearance and by the fact that they are not lined by endothelium-like cells.

The photomicrographs with their legends present my observations and interpretations better than any written description. These constitute the most important part of this paper. They also demonstrate both the value and the shortcomings of this method of study. I desire others to draw their own conclusions not only from a study of the photomicrographs in this paper, but of much greater importance, from the study of similar material of their own in which, if possible, the lymphatics have been injected. I have found a reading glass of great value in the study of the photomicrographs.

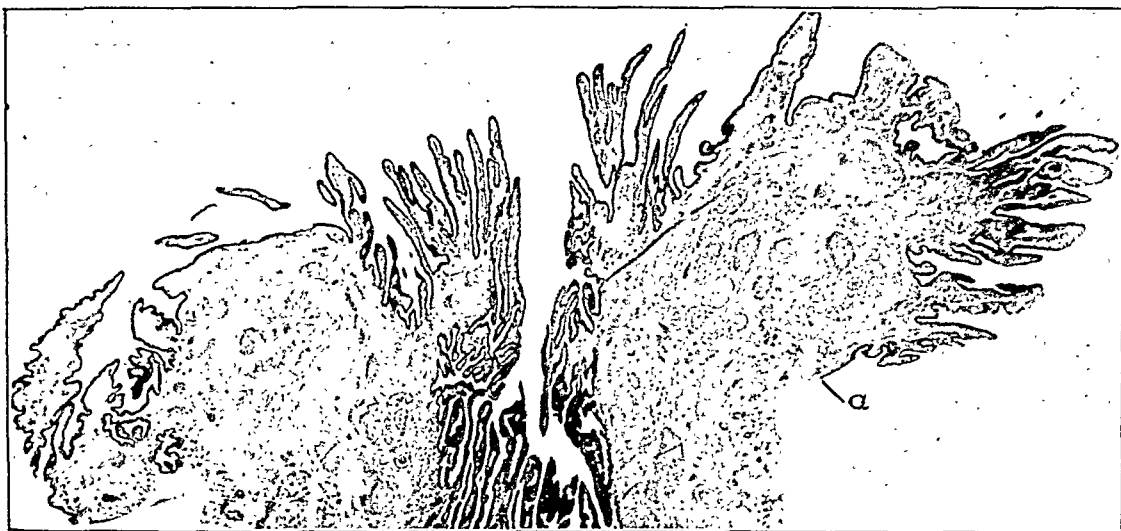


Fig. 10.

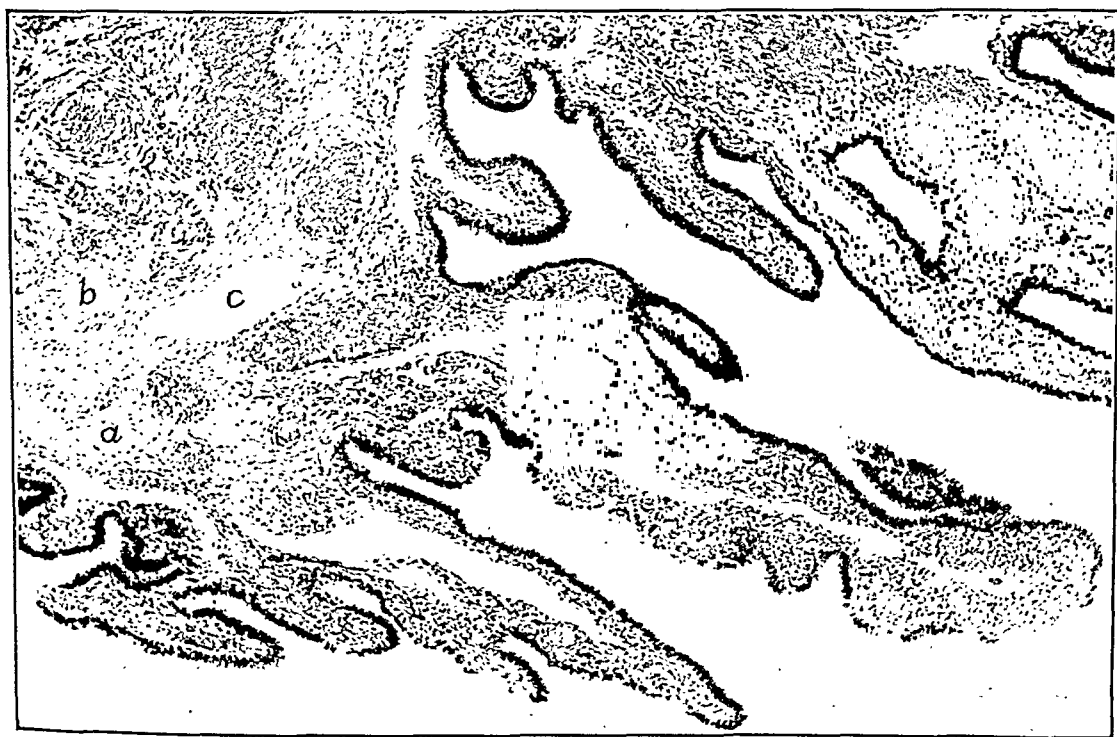


Fig. 11.

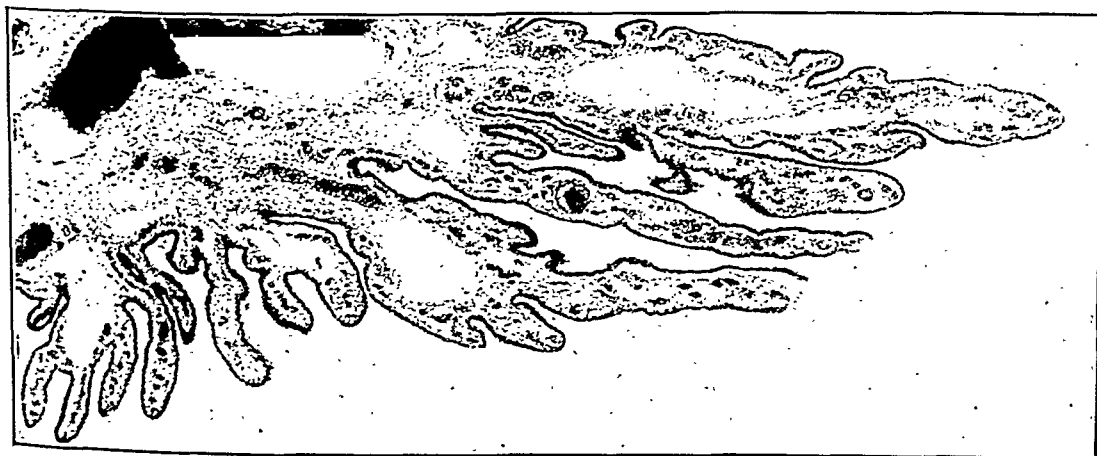


Fig. 12.

DISCUSSION

From the study of carcinoma-filled and empty lymphatics in the mucosa of the ampulla of the human fallopian tube, I believe that the distribution of these vessels in this mucosa closely resembles the distribution of the lymphatics in the mucosa of the ampulla of the sow's tube described by Andersen¹ (compare Figs. 2 to 6 with Fig. 1).

Since the fimbrial mucosa has the same histologic structure as the mucosa of the distal portion of the ampulla with which it is continuous one might infer that the distribution of the lymphatics in the mucosa in these two situations would be the same. This inference is correct as indicated in the photomicrographs (see Fig. 9 and compare Fig. 4 with Fig. 7, and Figs. 2 and 3 with Figs. 11, 12, and 13).

By comparing the lymph vessels in mucosal folds of approximately the same size and shape in one or in several sections of both the ampullar and fimbrial mucosa one is able, in a general way, to visualize the distribution of the lymphatics in that type of mucosal fold (see Figs. 4, 11, 12, and 20). Since mucosal folds vary in size and form the pattern of the lymphatics in these folds must vary accordingly. The larger folds with secondary folds arising from them will have a more complex lymphatic pattern than the smaller and simpler folds (Fig. 15).

For descriptive purposes the lymphatics of the ampullar and fimbrial mucosa may be divided into two plexuses: one situated in the mucosa at the base of and between the folds and the other in the folds. Vessels from the plexus in the folds empty into the plexus at the base of the folds. Thus the lymphatics of one mucosal fold are united with those of adjacent folds. This pattern prevails in all sizes and types of mucosal folds whether in the ampulla or fimbriae.

I have been unable to ascertain either the pattern of the branching and anastomosing of the lymph capillaries in the folds or the form of their termination (really origin) in the crest of the folds, whether the latter occurs in blind ends or loops. Only by a careful study of tubes in which the lymphatics have been injected can these finer and interesting details be determined. In the sections of the fimbriae studied by me the lymph vessels of the mucosa were usually more dilated and therefore more easily seen than the vessels in the ampullar mucosa of the same tube. In spite of this fact I experienced almost as much difficulty in tracing, even in serial sections, these noninjected capillaries in the fimbrial folds as I did in the ampullar folds.

Since the lymphatics of the ampullar and fimbrial mucosa are true capillaries without valves a free circulation of the lymph in all directions in the plexuses is assured.

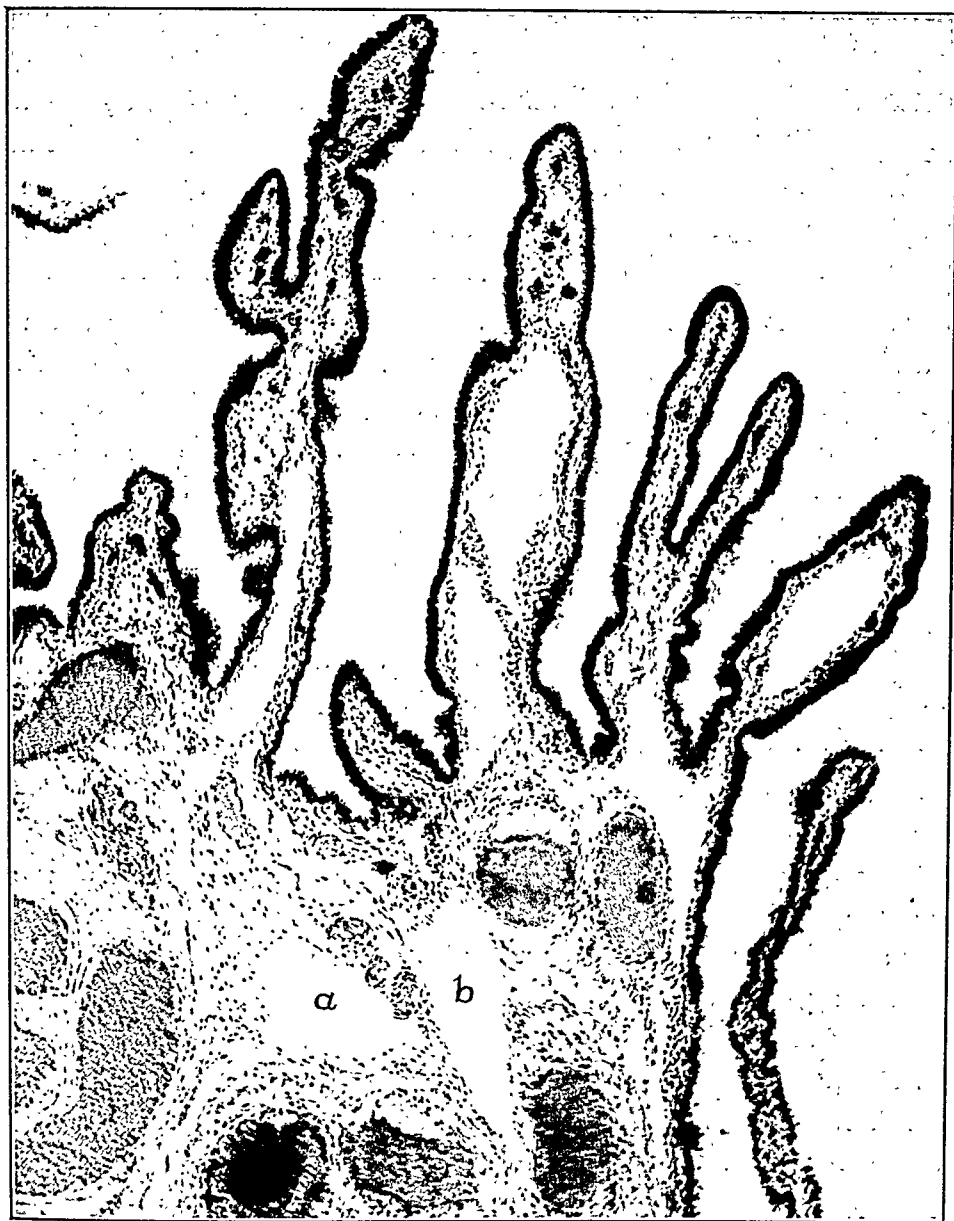


Fig. 13.



Fig. 14.

Fig. 16.—Cross-section of the fimbriae of a normal appearing tube at the level of its abdominal ostium (see Fig. 10 as a guide for the plane of this section). The patient, A. H. No. 970-32, parous, aged forty-nine, had had the uterus removed for benign uterine bleeding and descensus of that organ. The pelvic floor was also repaired for the results of the injuries of childbirth. The mucosa of the fimbriae covers over two-thirds of the surface of the circumference of the tube in this section. The lymph vessels of the mucosal folds of the fimbriae are greatly dilated as are those of the fimbriae shown in Fig. 19. $\times 5$.

Fig. 17.—Higher magnification of the fimbria in the upper right-hand portion of the section shown in the preceding photomicrograph. The veins, partly or completely filled with blood which stains darkly, can be easily seen. I believe that all of the empty spaces are the lumina of lymph vessels. By using a reading glass one can easily see the lymphatics, at the base of and between the folds, which drain the greatly dilated lymphatics of the folds and in turn empty into vessels in the stroma of the fimbria proper beneath them. $\times 25$.

Fig. 18.—Higher magnification of the fimbrial mucosa at its junction "a" with the serosa appearing in the left-hand portion of the section shown in Fig. 16. Note the dilated lymphatic, beneath the epithelium, which in this section appears to end blindly with the termination of the mucosa. In the examination of numerous sections, from many tubes, I have been unable to observe an anastomosis between the mucosal and the subserosal lymphatics. On the other hand, I have observed, in many sections, indications that the lymphatics of the terminal portion of the fimbrial mucosa are drained by vessels penetrating the tubal wall. $\times 54$.

There is abundant evidence that the lymphatics at the base of and between the mucosal folds of the fimbriae about the ostium of the tube are continuous with similar lymphatics of the mucosa of the distal portion of the ampulla (see Figs. 6, 9, 13, and 14). Also when a fimbrial mucosal fold is a continuation of a longitudinal fold of the ampulla the lymphatics in the folds as well as at their bases should be continuous (Fig. 9). Therefore some of the drainage of the lymphatics of the fimbrial mucosa must be through the lymphatics of the mucosa of the ampulla.

There are indications that the mucosal lymphatics of the fimbriae drain into vessels in the wall of the infundibulum and also in the mesosalpinx beneath this mucosa just as the lymphatics of the ampullar mucosa drain into vessels penetrating the wall of the tube beneath it.

I have not been able to detect any evidence of an anastomosis between the lymphatics of the fimbrial mucosa and the subserosal lymph vessels at the mucoserosal junction even in fimbriae in which the mucosal lymph vessels were filled with carcinoma (see Figs. 18, 20, and 21). Subserosal lymph vessels in this situation could not be detected in any of my sections. This may have been due to the normal scarcity of lymphatics beneath the serosa of the distal portion of the ampulla.

In only one instance could I detect any suggestion of the possibility of an anastomosis between the lymph vessels of the ovarian fimbriae

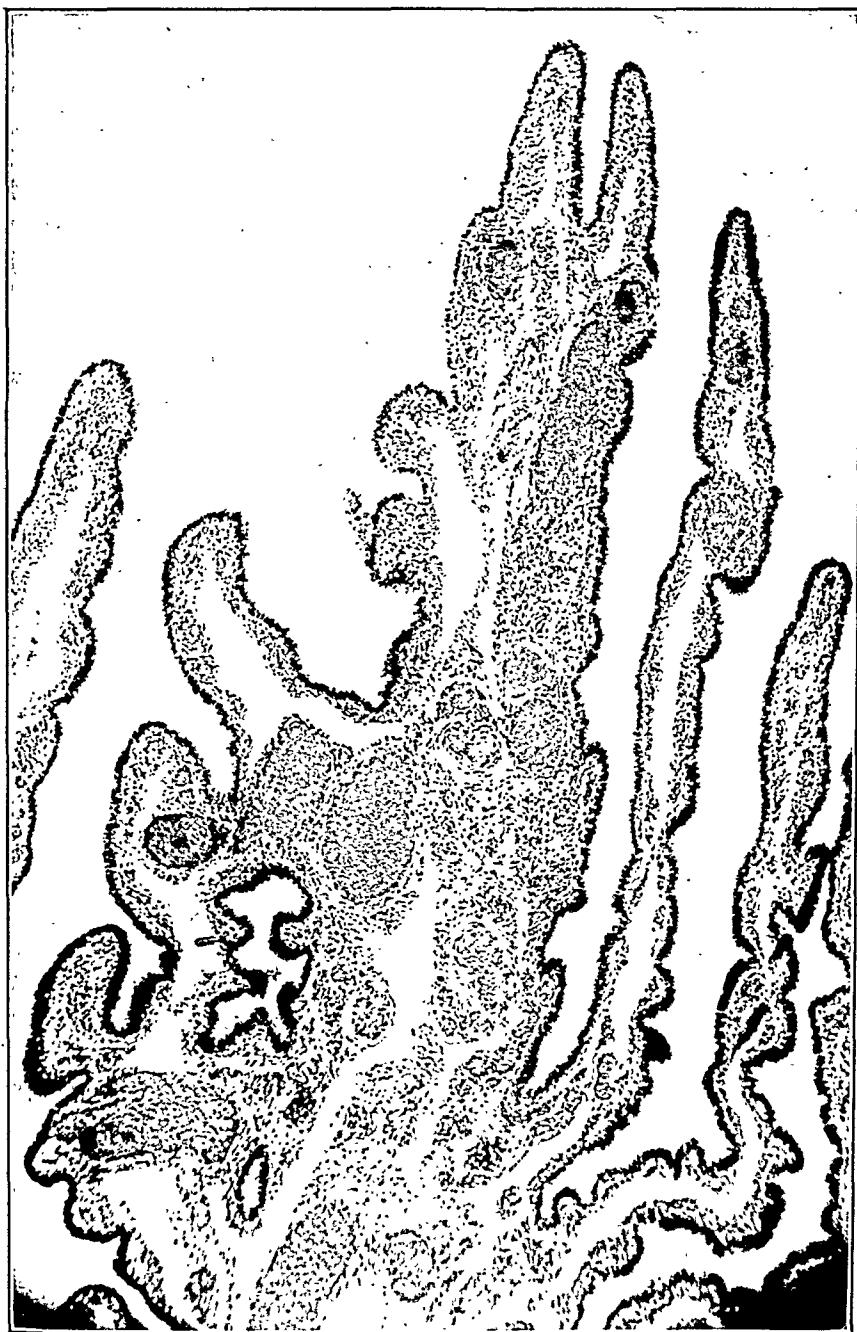


Fig. 15.—A large primary mucosal fold of the fimbriae with many secondary folds, from the section shown in the two preceding photomicrographs. Note the complexity of the pattern of the lymph vessels in the large fold and its relative simplicity in the secondary folds. The vessels in the secondary folds empty at their base into the lymph vessels of the large fold just as the lymph vessels of a primary fold drain into the lymph vessels at its base. $\times 50$.

Fig. 19.—Longitudinal section of the distal portion of a normal appearing tube, including its fimbriae proper, the free margin of the mesosalpinx with its ovarian fimbriae and a small portion of the ovary at the right. The patient, A. H. No. 8389-31, parous, aged forty-three, had had the entire uterus and one tube and ovary removed for multiple uterine leiomyomas. Lymphatics cannot be detected in the compressed mucosal folds of the ampulla. On the other hand the lymph vessels in nearly all of the mucosal folds of the fimbriae are greatly dilated and are therefore conspicuous. Note the great variation in the form and height of the mucosal folds. An anastomosis between the lymph plexus at the base of the folds of the ovarian fimbriae and the ovarian lymphatics cannot be detected. The latter are not evident. $\times 5$.

Fig. 20.—Higher magnification of mucosal folds of the fimbria in the left-hand portion of the section shown in the preceding photomicrograph. The lymphatics of the mucosa are easily seen. They do not extend beyond the mucoserosal junction (at the right). There is no evidence of any anastomosis between them and those of the subserosa. The latter lymphatics are not evident. The judged lymph vessels "a" and "b" in the tube possibly may drain the nearby mucosal lymphatics. $\times 54$.

Fig. 21.—Longitudinal section of a portion of the fimbriae of a tube with the mucosal lymph vessels filled with carcinoma as with an injection mass. The patient, A. H. No. 113036, parous, aged forty-nine, had had both tubes and ovaries and the uterus removed for carcinoma of both ovaries associated with an extensive peritoneal carcinomatosis. The carcinoma in this section is, for the most part, confined to the mucosal lymphatics. In places, however, it has extended beyond these vessels and invaded the tissues of the folds. Carcinoma in lymph vessels of the stroma of the infundibulum is indicated by the pointer "a." A mucoserosal junction is indicated by the letter "b." Note that carcinoma is present in the mucosal lymphatics almost up to the mucoserosal junction. The subserosal lymphatics are not evident. If carcinoma were present in the subserosal lymphatics in this situation it would indicate or at least suggest an anastomosis between them and the mucosal lymph vessels. I have never found carcinoma in the subserosal lymphatics in other specimens similar to this one. Note that the pattern of the carcinoma-filled lymph vessels of the mucosa near its junction with the serosa is similar to that shown in the preceding photomicrograph. Many blood vessels are present in the tissues of the infundibulum but very few recognizable lymph vessels. The observations presented in this paper form a chapter in the study of carcinoma of the tubal mucosa secondary to carcinoma of the ovary. Is lymphatic permeation and embolic metastasis by way of the lymph vessels from the ovarian tumor the only way that the carcinoma in the ovary can gain access to the mucosal lymph vessels of the tubal fimbriae? I hope to answer this question in a later paper. $\times 10$.

and lymph vessels coming from the hilum of the tubal pole of the ovary. In sections of this specimen judged lymph vessels accompanying blood vessels could be seen coming from the ovary into the tissues of the mesosalpinx beneath the ovarian fimbriae and also judged lymph vessels extending from the ovarian fimbriae toward the ovarian lymph vessels. Whether or not an anastomosis occurred between these two sets of lymph vessels could not be determined.

It would seem that lymph plexuses as rich and apparently as purposeful as those present in the fimbrial and ampullar mucosa must have some important function other than to furnish channels in which carcinoma may grow and spread.

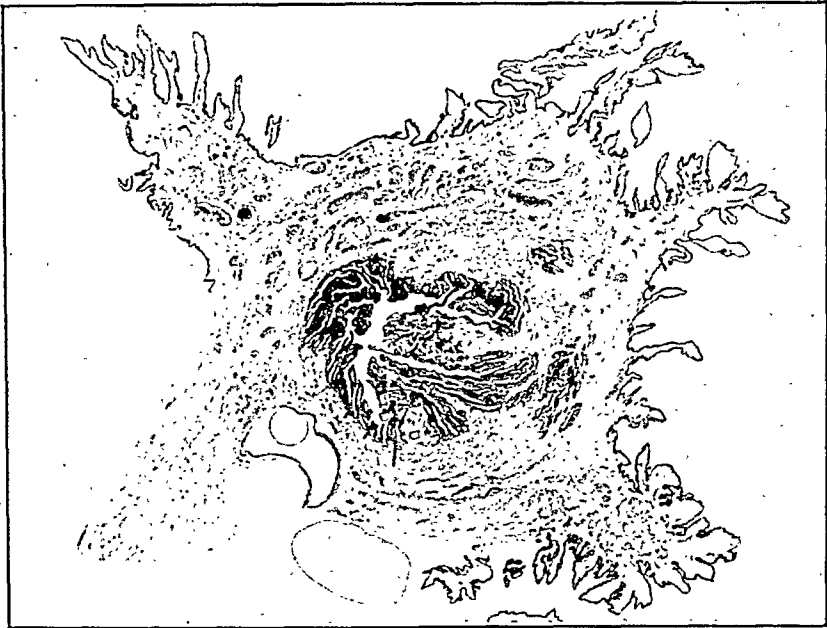


Fig. 16.

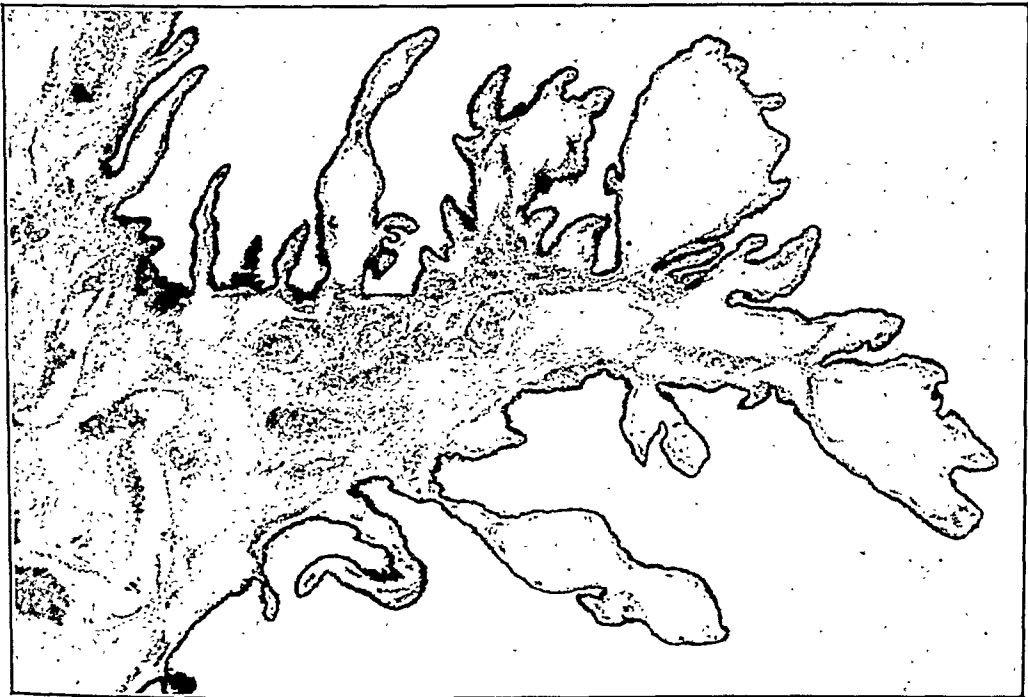


Fig. 17.

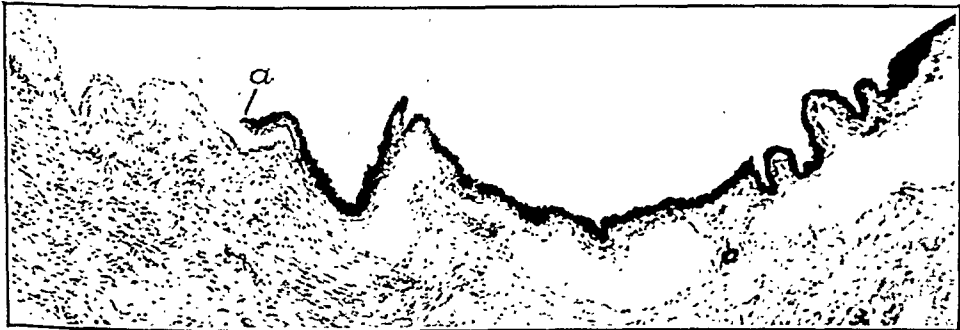


Fig. 18.

CONCLUSIONS

The mucosa of the fimbriae of the fallopian tube is richly supplied with lymphatics which are continuous with similar vessels in the mucosa of the distal portion of the ampulla of the tube.

The lymphatics of the fimbrial mucosa also drain into lymph vessels in the wall of the infundibulum of the tube and those of the ovarian fimbriae drain into lymph vessels in the mesosalpinx.

An anastomosis between lymph vessels, coming from the hilum of the tubal pole of the ovary, and the lymphatics of the adjacent ovarian fimbriae may well exist but was not positively demonstrated.

No suggestion was found of an anastomosis between the mucosal lymphatics of the fimbriae and the subserosal lymphatics at the mucoserosal junction.

NOTE: The efficiency of the laboratory work in the preparation of this paper is, in large measure, due to the technical skill and interest of Miss Helen Buchan and Miss Winifred Lansing. The photomicrographs were made by Mr. James A. Glenn. These I thank for their interest and cooperation.

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Fig. 19.

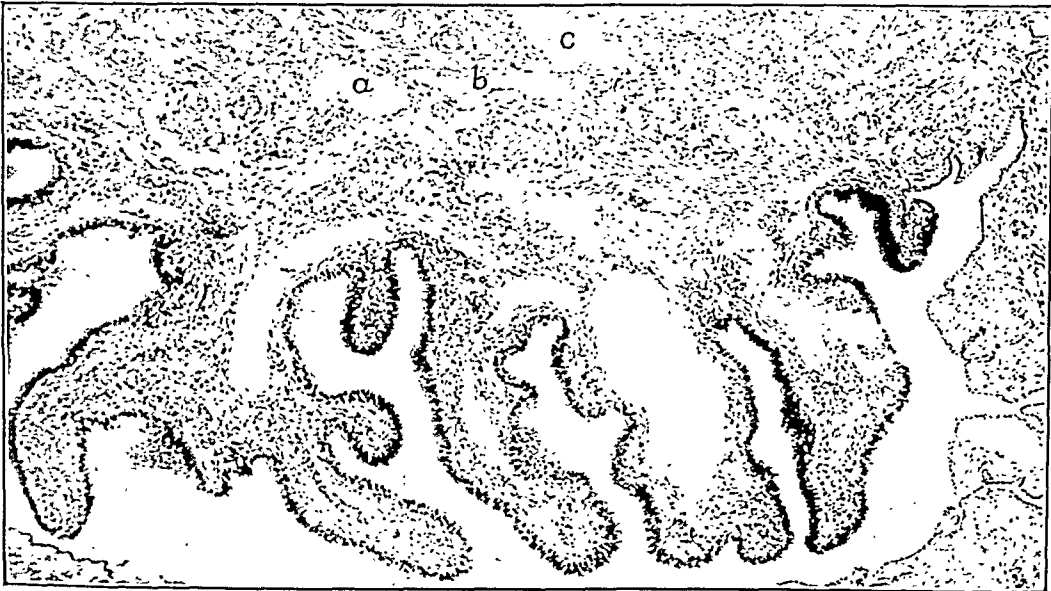


Fig. 20.



Fig. 21.

TYPES OF GONADOTROPIC HORMONES

With the announcement of Aschheim and Zondek that the injection of urine from pregnant women into immature rodents results in follicle growth and luteinization in the ovaries, it was at once assumed that it contained a principle derived from the anterior hypophysis. Although Engle, Orban and Watrin, and Collip early expressed doubt as to the validity of this conclusion, it was at once generally accepted and is still maintained by a number of authors. The work of the past few years, however, has brought forth a convincing array of facts which show that we are not dealing with a single anterior pituitary factor, but with a number of gonadotropic substances which may not have a common origin. I have summarized the most significant biologic differences between these hormones in a number of previous communications (Fluhmann¹¹⁻¹³), and they indicate that such substances should be identified with one or the other of two important groups.

1. The "anterior pituitary sex hormones" are found in the blood and urine of normal women and in increased amounts in castrates, in some patients with amenorrhea, and in the postclimacteric period. Their prototype is found in various extracts prepared from anterior pituitary glands or in fresh hypophyseal tissue, and two noteworthy biologic reactions may be mentioned. In immature rats or mice they induce a rapid development of numerous follicles, some of which luteinize while others undergo atresia, so that in 96 or 120 hours, the ovary presents the picture of numerous small corpora lutea interspersed with atretic follicles. Second, they readily stimulate follicle growth, luteinization and hypertrophy of interstitial cells in the ovaries of hypophysectomized rodents. Following the work of Hisaw, Fevold, and their collaborators, and subsequent corroboration from Wallen-Lawrence, Evans and others, it is now believed that these changes are due to two distinct hormones which may exist in various proportions. In the first place there is anterior pituitary hormone-A, which stimulates the growth and maturation of graafian follicles. Second, there is anterior pituitary hormone-B, which causes a luteinization of granulosa and thecal cells.

2. The "chorionic gonadotropic hormone" is distinct from the first group in that it occurs in large amounts during pregnancy, in association with chorion-epithelioma and hydatidiform mole, and in men with certain testicular tumors. It presents many biologic differences from the anterior pituitary hormones. For instance, in the immature rat ovary it induces follicle growth and luteinization, but the resultant histologic picture is characteristic. Instead of the large numbers of small, closely packed corpora lutea and atretic follicles which result from the administration of anterior lobe extracts, there are large corpora, normal developing follicles, and larger or smaller cysts lined with lutein cells. Moreover, these changes are believed to be due, not to the chorionic hormone alone, but to its action along with anterior pituitary factors already present in the normal animal. This is shown by the fact that in hypophysectomized rats the chorionic hormone fails to stimulate follicle development and only directly affects the ovarian interstitial cells. In spite of the repeated statement that the chorionic hormone is made up of two different elements (Novak¹⁴), no sound experimental evidence such as has been advanced for the anterior hypophyseal substance is as yet available.

THE DEMONSTRATION OF GONADOTROPIC SUBSTANCES IN THE BLOOD AND URINE

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AMONG the many medical contributions of Dr. Robert Tilden Frank, one of the most outstanding is the development of methods to demonstrate the presence of estrogenic hormones in the blood and urine. The importance of this work lies not altogether in the additions made to our knowledge, but also in the recognition of a new method of approach in studying problems of physiology and pathology. It seems particularly appropriate, therefore, in a volume dedicated to him and to his achievements, to consider the present status of our knowledge in an associated field, namely, the detection of gonadotropic substances in the blood and urine.

The basis for these studies was laid in 1921 when Evans and Long¹ succeeded in producing very definite changes in the reproductive system of the white rat by the intraperitoneal injection of an alkaline preparation of bovine anterior hypophyseal substance. A few years later Smith,² and Smith and Engle³ in this country, and Zondek and Aschheim⁴ in Germany, observed that inoculations of fresh anterior pituitary gland tissue into immature mice and rats leads to a precocious sexual maturity. In 1928 Aschheim and Zondek⁵ described their "pregnancy test" and showed that the urine of pregnant women contains large amounts of some hormone which has the property of inducing changes in the ovaries of laboratory animals. A standard procedure for the detection of gonadotropic hormones thus became available, and they were found in many body tissues and fluids under varying conditions. In 1929, Fels⁶ and Fluhmann⁷ noted their presence in the blood of pregnant women, Rössler⁸ in the urine of women with chorionepithelioma, Fluhmann⁹ in the blood of women following castration, in certain cases of amenorrhea and in the postclimacteric period, and Zondek¹⁰ in 1932 described their appearance in the urine of men with teratomas of the testicle. Since then, many reports have appeared which have given us valuable information regarding the production of these substances, their properties and distribution, and many refinements in the technic of the test. In the Stanford Laboratory of Gynecology over 3,000 tests for gonadotropic hormones in blood, urine, and tissue extracts have been conducted between 1928 and 1937.

be remembered, however, that any changes affecting the uterus and vagina are secondary to ovarian changes, and therefore cannot be employed unless it has been very clearly demonstrated that the material being tested does not contain any estrogenic substances. As a case in point, Thomsen and Pedersen-Bjergaard¹⁷ use the vaginal responses obtained in the mucification test for estrogenic substances (Fluhmann¹⁸) as criteria for stimulation of ovarian function in immature mice. It may no doubt prove a very delicate procedure for detecting gonadotropic hormones but is entirely dependent on the absolute absence of estrogenic hormone in the material originally administered to the animals. The final test for a gonadotropic hormone must depend on the clear demonstration of not only functional, but anatomic, changes in the ovary of the immature rodent. This is best shown by serial sections of ovaries fixed in Zenker's solution, mounted in paraffin, and stained by hematoxylin and eosin.

Two such effects are of significance in testing for the anterior pituitary gonadotropic hormone; (1) developing, or large atretic graafian follicles, and (2) corpora lutea, with or without imprisoned ova.* In the majority of instances, large follicles with or without signs of atresia in the ovary of the test mouse give evidence of anterior lobe gonadotropic hormone in the blood or urine. On the other hand, luteinization occurs also and is apparently dependent on a quantitative factor, although there is the possibility that it is due to a relative concentration of the "follicle-stimulating" and "luteinizing" hormones of the anterior lobe. In 71 positive tests with blood serum I found 15 instances of corpus luteum formation (Fluhmann¹⁹), and similar observations have been made by a number of other workers. Salmon and Frank²⁰ recently investigated this aspect of the problem, and rightly pointed out that either follicle-stimulating or luteinizing effects could be produced in immature (rat) ovaries by increasing or decreasing the dosage of given extracts, but it was not possible "to conclude whether one factor at different dosage produces both effects or whether two factors are present with different dosage thresholds."

The administration of untreated blood serum or urine from normal individuals to immature mice or rats fails to yield positive tests. The blood of 45 women with normal menstrual cycles regularly gave negative reactions (Fluhmann¹⁹), and Mazer and Goldstein²¹ obtained positive results in only 2 out of 53 similar patients. This method is therefore of no use in studying the normal content of gonadotropic substances in blood or urine, although it is of distinct value in demonstrating increases of the hormone under various conditions. For this

*In addition, mention must be made of follicles with hemorrhage (APR-II of the original A-Z reactions) and lutein cysts, but these appear infrequently and are more characteristic of the chorionic hormone.

The origin of the chorionic hormone is not known for a certainty. In many ways it seems to fulfill the requirements for a luteinizing factor from the anterior hypophysis, but on the other hand, there is good reason to believe that it may be produced by the placenta and by certain newgrowths. Until the final answer is obtained, it is very important that these two groups be kept distinct, and this is especially true in dealing with clinical problems. There are not only many biologic differences between the two types of hormones, but they also occur under very different physiologic and pathologic conditions.

ANTERIOR PITUITARY GONADOTROPIC HORMONES

The demonstration of this type of gonadotropic hormone depends on the employment of various modifications of the Aschheim-Zondek pregnancy test. Mice, rats, or rabbits may be used. The relatively small size of the mouse makes it a more sensitive test animal but a marked disadvantage is faced when extracts with toxic properties are injected. With any extensive studies of this nature it is desirable that a colony of mice be developed so that exact ages may be known and control observations made at different seasons to determine the time at which first estrus appears in the majority of animals. The work of Engle and Rosasco¹⁵ and Hamburger¹⁶ has amply shown the many errors which may arise from the common practice of purchasing mice from dealers and depending altogether on body weight as evidence of immaturity. In the Stanford Laboratory of Gynecology it has been found necessary to begin the test with mice eighteen to twenty days old, since sexual maturity occasionally may appear as early as twenty-five days of age.

The injections have been carried out in various ways, but two methods may be mentioned as standard procedures. First, the material to be tested may be given in single daily doses for three consecutive days and the animals sacrificed in 96 to 100 hours from the time of the first injection. This is generally done with extracts, but whenever blood serum or urine is tested directly, it is preferable to give a larger number of injections and to prolong the period of observation. For instance, in examining blood serum it has been our practice to inject 0.5 c.c. twice daily for four consecutive days and to autopsy the mice in 120 hours from the beginning of the experiment.

The end point of the test designating a positive result has received many interpretations. The stimulus of the gonadotropic hormone causes follicle development with or without luteinization in the ovary, and secondarily, enlargement of the uterus, establishment of the vaginal introitus, and estrous changes in the vaginal mucosa. It must

increase was observed as early as eight days following operative castration, and Österreicher⁴⁶ and Saethre⁴⁷ have demonstrated it in the urine of women as old as eighty and ninety years of age.

This observation is of considerable interest and two possibilities arise to explain the great increase of the hormone in the blood and urine. It may result from a nonutilization of the hormone by afunctional or absent gonads, but a number of associated findings support the view that it is due to an actual hyperfunction of the anterior hypophysis. (1) It is in keeping with the postcastration hypertrophy of the anterior lobe of women, which has been described by a number of authors (Tandler and Gross,⁴⁸ Kon,⁴⁹ Kolde,⁵⁰ Rössle⁵¹). (2) Anterior hypophyseal tissue from gonadectomized rats is much more potent to stimulate the ovaries of immature rodents than that from normal controls (Engle,⁵² Evans and Simpson⁵³). (3) Estrogenic hormones are inhibitors of anterior pituitary function so that this inhibition is removed with the cessation of ovarian function. (4) It has been possible to decrease the excessive elimination of gonadotropic hormone in menopausal patients by the administration of large dosages of estrogenic substances (Albright,⁵⁴ Frank and Salmon,⁵⁵ Zondek⁵⁶).*

In the light of these findings the demonstration of excessive amounts of anterior lobe gonadotropic hormone in the blood and urine of women is interpreted as indicating a cessation of ovarian function and has been employed in a number of clinical problems. For instance, it is of value in the study of patients with amenorrhea, and positive tests are considered as evidence of a "primary ovarian failure" (Mazer and Goldstein²¹). It also has been used recently to determine the duration of gonadal function in women who have had hysterectomy with conservation of the gonads (Marx and others,⁵⁷ Tamis⁵⁸).

It has been maintained that an increased elimination of anterior lobe gonadotropic hormone occurs in two important conditions in addition to lack of ovarian function. In the first place, Zondek⁵⁹ has reported its association with carcinoma of various pelvic organs in a large proportion of cases, and apparent corroboration has come from Winter⁶⁰ and Bandler.⁶¹ However, these findings have not been substantiated by Frank⁶² and Hamburger,⁶³ and in my own studies with blood no relation could be found between carcinomatous disease and increase of gonadotropic hormone in younger individuals. It must be

*However, the exact relationship between estrogenic hormones and overproduction of anterior lobe gonadotropic substances is not quite clear. It has been maintained that the latter occurs with the disappearance of the ovarian factors, but that is not necessarily true. A certain percentage of preclimacteric patients show an increase of gonadotropic hormones while still menstruating, and recent studies indicate that estrogenic substances are found in both castrates and postmenopausal women. The two groups of hormones may thus be present in large amounts at the same time.

reason, a number of procedures have been developed to concentrate the amount of hormone present before the biologic test is conducted. Neumann and Peter,²² Frank and Salmon,²³ and Freed²⁴ have described methods of extracting gonadotropic substances from blood, and similar procedures for urine have been reported by Zondek,²⁵ Katzman and Doisy,²⁶ Levin and Tyndale,²⁷ Katzman,²⁸ and others. Although the exact relationship between gonadotropic hormones in the circulating blood and those excreted in the urine has not been established by careful analysis, it is generally believed that they run parallel and are directly comparable.

There is, unfortunately, no uniformity of results in the studies conducted on the presence of gonadotropic hormones in the blood and urine of normal individuals. Soeken²⁹ reported positive tests in the urine of 24 out of 50 children, but his findings could not be corroborated by Schörcher³⁰ and Ehrhardt and Ruhl.³¹ Katzman and Doisy²⁶ observed that between the ages of four years and puberty little or none of the gonadotropic substance was found, while at puberty an increased excretion occurred. The examination of the blood and urine of normal menstruating women also shows much contradiction. Frank and others³² found that a maximal concentration of gonadotropic substances in the blood occurred from the sixth to the ninth days of the cycle, Frank and Salmon²³ from the ninth to the thirteenth days, while Neumann and Peter³³ noted an increase during the premenstruum. The studies conducted with urine are likewise confusing, but the available reports may be placed in two groups. In the first are those investigators who believe that the maximal excretion of gonadotropic hormone takes place during the premenstruum (Zondek³⁴ and Österreicher³⁵). The second group (Katzman and Doisy,²⁶ Kurzorok and others³⁶) finds the greatest concentration at about the middle of the menstrual cycle and feels that it represents an increased activity of the anterior lobe which is associated with ovulation. It is hoped that additional data on these important points will soon be available.

Although difficulty has been experienced in determining the occurrence of anterior pituitary gonadotropic hormone under normal conditions, it has been amply demonstrated that following a loss of ovarian function there is a marked increase both in the blood (Fluhmann,⁷ Zondek,³⁷ Mazer and Hoffman³⁸), and in the urine (Zondek,³⁹ Jeffcoate,⁴⁰ Mazer and Andrussier,⁴¹ Brühl,⁴² Österreicher,⁴³ Gostimirove,⁴⁴ and others). In my original studies,^{7, 19, 45} an increase of gonadotropic hormone in the blood was found in 40 per cent of patients examined within three months after an operative castration and in 76 per cent after this period, in 60 per cent of women following an irradiation castration, in 60 per cent of postmenopausal women, and in a number of patients with long periods of amenorrhea. This

and we employ animals of from twenty-one to twenty-three days of age which have been bred in our own colony. Since the chorionic hormone usually occurs in very great amounts it is not necessary to concentrate either the urine or the blood, and, in fact, in doing quantitative tests it is usually necessary to dilute the original specimens. At least three rats should be used for each dosage level, and according to the original Aschheim-Zondek procedure 3 injections are given daily for two days and the animals sacrificed in 96 to 100 hours. Although some of the changes induced in the ovaries may be detected grossly, it is much better to study serial sections as in the case of the anterior pituitary gonadotropic substance. Three reactions have been described. "APR-I" is denoted by the presence of follicles, and these consist of normal developing follicles or small cysts lined with lutein cells. There is a striking absence of follicles showing chromatolytic degeneration, as seen with anterior lobe preparations. "APR-II" consists of hemorrhages into follicles or lutein cysts, and may be seen grossly as "Blutpunkte," but they do not occur as readily in rats as in mice. "APR-III" is indicated by corpora lutea, with or without imprisoned ova.

The chorionic hormone is not found in normal menstruating women, but occurs in very great amounts throughout the whole course of gestation in the human. It may be observed as early as during the first two weeks following conception, but it rapidly disappears within a few days after delivery. It is beyond the scope of this review to refer to the numerous studies on the amounts of hormone present at different stages of pregnancy, but attention must be directed to the recent careful work of Evans and his associates.⁷⁵ These authors emphasize two of their observations which have considerable clinical significance. In the first place, the amount of hormone in the urine maintains a high level throughout pregnancy, but there occurs an exceedingly steep hormone peak at a time which is quite accurately one month from the beginning of the first expected but missed menstruation. Second, they find hormone levels associated with normal gestation far greater than previously reported. In one case, over one million rat units were excreted during the course of twenty-four hours.

The wide variations of hormone levels encountered in different individuals, the high peaks observed by Evans, and the difficulties of accurate quantitative determinations render it very difficult to efficiently control any analysis of increase or decrease in the amounts of hormone present in pathologic conditions. It is of particular interest, however, that a number of investigators have reported excessive amounts of the chorionic substance in the blood and/or urine in hyperemesis gravidarum (Von Weymersch,⁷⁶ Anker and Laland,⁷⁷ Schoeneck,⁷⁸ Heim,⁷⁹ Ehrhardt,⁸⁰ Anselmino and Hoffmann⁸¹) and in the

pointed out, also, that the vast majority of reported positive results occurred in women in the preclimacteric or climacteric periods. Second, considerable discussion has centered on the presence of gonadotropic hormones in the urine of patients with acromegaly, hypophyseal tumors, prolonged increase of intracranial pressure or essential hypertension. In these instances there is likewise a diversity of opinion, positive tests having been reported by v. Morgitay-Becht and Miklos,⁶⁴ Kraus,⁶⁵ Hirsch-Hoffmann,⁶⁶ Kylin,⁶⁷ and McCullagh and Cuyler,⁶⁸ while Watts,⁶⁹ Fels,⁷⁰ and Scarf and Israel⁷¹ have not been able to offer corroborative evidence. This aspect of the question should therefore remain sub judice for the present and await further studies.

CHORIONIC GONADOTROPIC HORMONE

The Aschheim-Zondek "pregnancy test" is the method employed for the detection of the chorionic gonadotropic hormone, and it has received widespread acceptance as a standard procedure. In this country the use of rabbits, as suggested by Friedman, has supplanted rats and mice as test animals, and the many writers who have reported on the subject attest to its great accuracy. The modified Friedman test employed in the Stanford Laboratory of Gynecology has given 99 per cent correct results in normal pregnancy, and our experience supports the recommendations recently made by Kelly and Woods.⁷² The patients are instructed to limit fluid intake after 10:00 P.M. on the day previous to the examination, and the first specimen of urine voided the following morning is forwarded to the laboratory. The rabbits are adult females weighing no less than 3½ pounds, which have been isolated for a period of at least two days. They are anesthetized with ether, and a small incision is then made in the flank in order to inspect one of the ovaries. If small clear follicles are found, the ovary is dropped back into the abdominal cavity and the wound closed by interrupted stitches in the muscles and metal clips in the skin. An intravenous injection of 7 c.c. of the urine is made at once into one of the ear veins, and this is repeated a few hours later. The rabbits are examined forty-eight hours after the first injection, and a positive result is made from the presence of hemorrhagic or ruptured follicles in one or both ovaries.

Although the Friedman test is the method of choice for the routine examination of urine specimens, there is still a field of usefulness for the smaller rodents in making quantitative determinations of the hormone or for the study of blood or tissues. In contrast to the anterior lobe gonadotropic hormone, however, the rat is from 3 to 5 times more sensitive than the mouse to the chorionic substance (Hamburger,⁶³ Rowe and others,⁷³ Nelson and Overholser⁷⁴). The same precautions should be employed in choosing suitable immature rats,

tumor. In a recent communication, Hamburger⁹⁴ maintains that in addition to the group of newgrowths which produce the chorionic hormone, seminomas of the testis may also cause the appearance of a gonadotropic factor which has the characteristics of the anterior lobe follicle-stimulating hormone.

The development of methods to detect gonadotropic hormones in the blood and urine has contributed much to the progress of our knowledge. They have given us tests which not only are valuable for practical application but serve as guides in the investigation of obscure problems in physiology and pathology. In spite of the advances that have been made there is much to be accomplished in the future, and it is hoped that many more workers will adopt these procedures and contribute to this important field.

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toxemias of late pregnancy (Smith and Smith,⁸² Heim,⁷⁹ Anselmino and Hoffmann⁸¹). The significance of this increase is difficult of interpretation, but is an observation worthy of further investigation.

The demonstration of the chorionic gonadotropic hormone in the blood and urine of women with hydatidiform mole and chorionepithelioma has been accomplished by many workers (Rössler,⁸ Zondek,⁸³ Mazer,⁸⁴ Mack and Catherwood,⁸⁵ Kimbrough,⁸⁶ Mathieu and Palmer,⁸⁷ Zondek,⁸⁸ and others). It is a discovery of the utmost clinical significance and may be of great value from the standpoint of diagnosis and therapy. The occurrence of positive tests, and especially of tests increasing in intensity some weeks or months after a normal pregnancy or a hydatidiform mole, is very important in establishing a diagnosis of chorionepithelioma. It is also of inestimable significance in controlling therapeutic measures, since a persistence of the hormone in the urine may indicate an incomplete operation for a mole or the occurrence of metastases in chorionepithelioma. On the other hand, it must be recognized that there are some limitations to the usage of the test and the results must be clearly interpreted in the light of the patient's history. For instance, the chorionic hormone may persist in the blood and urine for as long as six weeks after the evacuation of a hydatidiform mole and therefore may not necessarily imply that an incomplete operation has been performed or that a chorionepithelioma is present.* It is also especially important to interpret with caution the results of quantitative determinations of the hormone. Zondek⁸⁸ states that the presence of 200,000 units or more of the luteinizing hormone in the urine favors the diagnosis of hydatidiform mole in the differentiation from a normal pregnancy. However, much higher values have been found in normal pregnancy; and again little or no hormone could be demonstrated in some instances of hydatidiform mole (Philipp⁸⁹). In a patient with a chorionepithelioma uteri associated with extensive metastases to the lungs and liver I found smaller amounts of the chorionic hormone in the urine than are generally present during the course of a normal gestation.

The presence of a gonadotropic principle in the urine of men with teratomas of the testicle was first reported by Zondek⁹⁰ and has received abundant confirmation from Ferguson⁹¹ and others. It also has been recently shown that this substance has the biologic properties of the chorionic and not of the anterior hypophyseal hormone (Fluhmann and Hoffmann,⁹² Evans⁹³). The test in such cases is of value in the differential diagnosis of testicular tumors and may be employed to determine the effectiveness of operative or irradiation therapy and the appearance of metastases following the eradication of the primary

*However, if the examination of the urine yields positive results after it has become negative, the finding is significant.

THE INFLUENCE OF LACTATION ON THE IMPLANTATION OF THE MAMMALIAN EMBRYO

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THE attachment of the embryo to the uterine mucosa constitutes a critical period both in the development of the embryo itself and in the maternal processes of gestation. Prior to implantation the embryo has no organic connection with the maternal tissues and is indeed isolated from them by the more or less attenuated zona pellucida, which persists in some forms almost until this time. It is dependent for its nutrition partly on the reserve materials of the ovum and partly on the contents of the fallopian tube and uterus, which are absorbed in fluid form. Subsequently the embryonic and maternal tissues are in continuity and the nutrition of the embryo is then effected by the absorptive and phagocytic activity of the trophoblast and of the placenta. Implantation marks in the mother the transition from the preparatory postestrous reconstruction of the uterine mucosa and the phase of maximum secretory activity of the uterine glands to the formation of the definitive maternal placental tissues. Despite the importance of implantation in gestation and the considerable knowledge we possess of the morphologic changes which accompany it, we know relatively little of the physiologic processes concerned. Some light is thrown on these by the observations on the effect of lactation in retarding implantation which are reviewed in this paper.

Lataste recognized in 1882 that, in a number of mammals, the duration of gestation is prolonged during lactation. In his treatise entitled "*Recherches de Zooéthique sur les Mammifères de l'ordre des Rongeurs*," (1887) he stated: "Chez les Muridés, quand la femelle entre en lactation au début de sa grossesse, la durée de la gestation peut être de trois périodes génitales; dans tous les autres cas, elle n'est que de deux périodes." The "période génitale" of Lataste's Law is the approximately ten-day period of the pseudopregnant or mated estrous cycle of the mouse.

Although Lataste's most extensive researches on this problem were performed on the mouse, he showed that gestation is prolonged by lactation in *Dipodillus Simoni*, Lataste, and *Meriones longifrons*, Lataste, as well. Moreover he showed conclusively that the prolongation is due to an arrest in the development of the embryos at an early stage, before they have produced macroscopically distinguishable swellings of the uterus. He states that lactation continued for only three, five, or eight days from the time of parturition does not result in prolongation of gestation, but examination of his schedules reveals that while this conclusion was justified for three and five days' lactation, it was not in the case of eight days' lactation. Lataste also

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retardations varying from two to twelve days. In another experiment involving sixteen mice, the animals were allowed to suckle the whole litter born at first but subsequently all but one were removed at intervals, varying from one to thirteen days *postpartum*. All were killed on the thirteenth day *postpartum* and the embryos examined. All the six that suckled the whole litter for more than six days, that is after the normal time of implantation, showed retardation of from five to eight days. Some of those that suckled the whole litter for six days or less exhibited retardation of up to five days while others showed none.

Mirskaia and Crew (1931) record the duration of pregnancy in 19 mice, suckling from 3 to 8 young, of which 7 were primiparas, having become pregnant at their first *postpartum* estrus, and 12 were multiparas. They found that in all cases gestation was prolonged, the period varying from six to sixteen days without reference either to the number of young in the uterus or suckling. They found no support for Kirkham's view that the functioning mammary glands exert an inhibitory action on the uterus, but they suggest that the delayed implantation is due to inability of the corpus luteum to provide sufficient luteal hormone for implantation and lactation to take place simultaneously.

Hain (1934) records variations between twenty-two and thirty-six days in the duration of pregnancy in fifteen albino rats suckling from 3 to 11 young. She concluded that, unlike the mouse, the duration of pregnancy in the rat may not be prolonged when only 3 or 4 young are suckled. It is always prolonged when more than four young are suckled. She found no correlation between the number of young suckled and the duration of the prolonged gestation. Hain found no evidence that the number of embryos in the uteri affects the duration of gestation when five or less young are suckled, as was suggested by King (1913).

Lataste's pioneer work seems to have been overlooked by all the subsequent workers referred to above, since in none of the papers quoted is there any reference to it.

The author (1935), when investigating the estrous cycle of the common shrew (*Sorex araneus*, Linnaeus) with material trapped in the wild state, found among the pregnant animals an unexpectedly high proportion with blastocysts free in the uterine lumen. In this species, it is possible to distinguish females that are pregnant for the first time from those that are parous, and further analysis revealed that this unexpected preponderance of the unimplanted uterine blastocyst stages was almost entirely confined to the group of parous females. Moreover in the common shrew the majority of females become pregnant at the *postpartum* estrus, lactating and gestating simultaneously. The distribution of the ninety-nine pregnant animals obtained, according to the stage of the contained embryos, between first and subsequent pregnancies, is summarized in Table I.

TABLE I

STAGE OF EMBRYOS	FIRST PREGNANCIES	SUBSEQUENT PREGNANCIES
Fertilized ova in the fallopian tubes	7	11
Blastocysts free in the uterine lumen	3	26
Implanted embryos	32	20
Total	42	57

showed that mammary activity below a certain intensity does not produce a retardation of development; thus the duration of gestation was normal in mice suckling only one or two young while it was prolonged in those suckling three or more young.

Daniel (1910) records ten instances of the prolongation of gestation from two to ten days in mice suckling from three to ten young. He concluded from these data that the period of gestation, in lactating mothers, varies directly with the number of young suckled. He found that the prolongation was approximately one day for each young suckled. Although his data are meager, they gain weight from the fact that only five females were used, three of which had two prolonged gestations and one had three. In each individual mouse, as well as in the series as a whole, the prolongation was greater, the greater the number of young suckled.

King (1913) showed that a similar prolongation of gestation during lactation occurs in the albino rat, *Rattus norvegicus albinus*, of the Wistar Institute strain. She records the duration of thirty-one pregnancies, varying from twenty-one to thirty-four days, in rats suckling from three to eleven young. In this strain the gestation period in nonsuckling females varies from twenty-one to twenty-three days. All females suckling six or more young had prolonged periods of gestation; of the nineteen rats suckling five or less young, gestation was not prolonged in the eight which subsequently gave birth to litters of five or less but was prolonged in the eleven which gave birth to litters of six or more. It is suggested that the suckling of a litter of six or more young lessens the food supply to the fetal young and so retards their development.

Kirkham (1916) investigated the stage of development attained by the embryos in a series of 21 mice suckling from three to eight young killed at daily intervals from six to twenty-four days *postpartum*. He compared these with a standard series of embryos from nonsuckling females which had become pregnant at the *postpartum* estrus. He found that copulation occurs within twenty-four hours of parturition and that in both suckling and nonsuckling animals the ova are in the 2-cell stage during the first and second days of gestation, are morulas during the third and fourth days and during the fifth day are blastocysts free in the uterine lumen. In nonsuckling females, in which the normal gestation period is twenty days, they become implanted at the close of the fifth day. Ten females suckling from three to eight young, when killed from six to fourteen days *postpartum*, all had blastocysts free in the uterine lumen. He concluded, therefore, that in the suckling mouse implantation occurs at the end of the thirteenth day of pregnancy (fourteenth day *postpartum*) and that this delay is due to the loss of surplus nourishment through the mammary glands, preventing the uterine mucosa from reacting to the embryos. The embryos in eleven suckling mice killed from fifteen to twenty-four days *postpartum* were implanted and exhibited retardation, compared with those of nonsuckling mice, of from three to fourteen days, except in the single instance where only 3 young were suckled in which there was no apparent retardation. He found no evident correlation between the amount of retardation and either the number of young suckled or the number of embryos in utero.

Kirkham, in a subsequent paper (1918), records the duration of pregnancy in nine mice suckling from one to four young. None of the four mice suckling one or two young showed any prolongation, four mice suckling three or four young showed prolongations of from nine to eleven days and one mouse suckling three showed none. A series of twenty-two mice, which were each suckling four young and were killed at intervals of from two to twenty-five days *postcoitum*, were examined, and the contained embryos were compared with those from nonsuckling females. None of those killed up to the thirteenth day had implanted embryos, whereas eleven of the twelve killed subsequently had. The eleven animals with implanted embryos exhibited

present issue, since it is the relative preponderance of free uterine blastocyst stages as compared with tubal stages in the group including all suckling females which indicates delayed implantation during lactation. There is thus very strong evidence that such delay occurs in this species.

Information regarding the growth of the corpus luteum during pregnancy in this species was obtained by measuring the diameters of the corpora lutea of pregnancy of all the animals available and calculating the mean diameter of those of each. By arranging the pregnant animals in order according to the stage of development of the contained embryos, from the earliest to the latest, and plotting the mean diameters of the corpora lutea against the position of the corresponding animal in this series it was possible to arrive at a graphical represen-

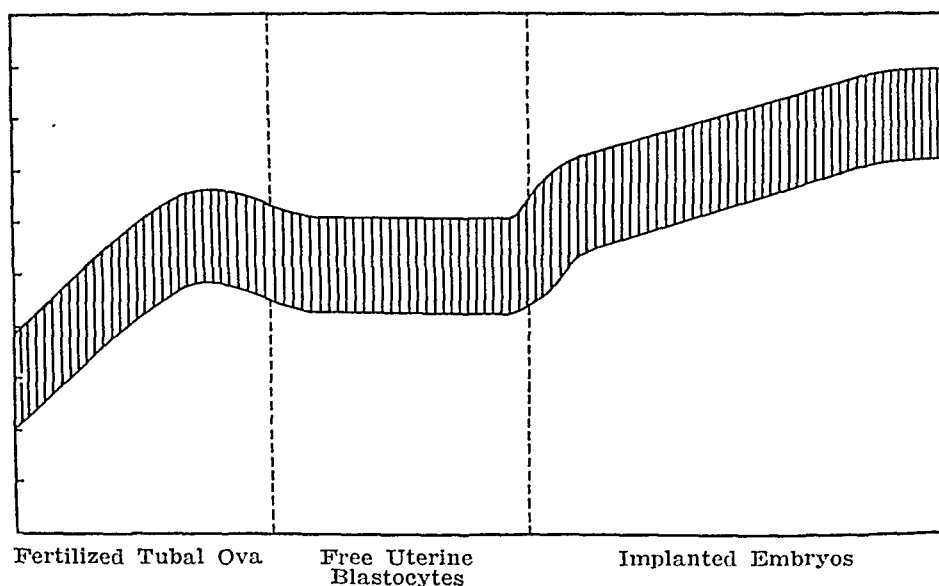


Fig. 1.

tation of the growth curve of the corpora lutea during pregnancy. This curve is represented diagrammatically in Fig. 1. It is apparent that the corpora lutea grow rapidly from the time of ovulation until the tubal ova are in the 8-cell stage. Thereafter there is no growth and there is even an indication of a slight decrease in size, until implantation occurs, when a second but less rapid growth phase begins and continues without interruption until parturition.

Assuming that, as in the mouse, without delayed implantation due to lactation, free uterine blastocyst stages should be one-fourth as numerous as tubal stages, and since there are 49 tubal stages, then the excess over twelve or approximately 75 per cent of the free uterine blastocyst stages must be assumed to be in a state of arrested development and delayed implantation due to lactation. The data on which Fig. 1 is based therefore clearly indicate that, when the development of the blastocysts is arrested and their sojourn free in

The relative durations of these three stages in nonsuckling shrews are not known, but it may be assumed for the present purpose that they do not differ widely from those in the mouse which Kirkham (1916) has shown to be approximately four, one, and fifteen days, respectively. We would expect, on this assumption, to find in a random sample of pregnant animals 20 per cent with fertilized tubal ova, 5 per cent with free uterine blastocysts, and 75 per cent with implanted embryos. The fact that in many species of wild mammals the pregnant females approaching full term are more difficult to trap, presumably because they are less active, provides a satisfactory explanation of the relatively small number with implanted embryos actually obtained. The relative numbers obtained of the two earlier stages cannot be accounted for in this way and are much more significant. The very much greater relative frequency of free uterine blastocyst stages in parous animals can be satisfactorily explained only by postulating an arrest in the development of the blastocysts and a delay in implantation during lactation such as occurs in the small rodents.

A similar prolongation of gestation during lactation probably occurs in the lesser shrew (*Sorex minutus*, Linnaeus) also, for among 47 pregnant animals, 4 had tubal ova, 12 had free uterine blastocysts, and 31 had implanted embryos (Brambell and Hall, 1937).

The bank vole (*Clethrionomys glareolus britannicus*, Miller) also exhibits a preponderance of free uterine blastocyst stages among wild pregnant females (Brambell and Rowlands, 1936). In this species it is not possible to distinguish parous animals from those pregnant for the first time, except in special instances. However, animals taken during the early part of the breeding season (in April and the first half of May) cannot have been suckling, whereas the majority of those taken later in the season were in lactation. Comparison of the number of tubal and unimplanted uterine stages in these two groups, as shown in Table II, reveals a very marked preponderance in the proportion of free uterine blastocyst stages in the latter part of the season.

TABLE II

STAGE OF EMBRYOS	BEGINNING OF SEASON TO MAY 15	MAY 16 TO END OF SEASON
Fertilized ova in the fallopian tubes	23	26
Blastocysts free in the uterine lumen	8	42
Total	31	68

This species appears much more difficult to trap in the later stages of pregnancy than the common shrew since of 179 pregnant animals obtained only 80 had implanted embryos. This does not affect the

The maximum of twenty-two days, observed in two instances only in animals suckling one or two young, cannot be regarded as a significant prolongation of the normal gestation period, since this is known to exhibit variations of one or two days, especially in animals

TABLE III

PROLONGATION IN DAYS	NUMBER OF YOUNG SUCKLED									
	1	2	3	4	5	6	7	8	9	10
16								1		
15							1			
14							1			
13				1	1	4				
12			1	3		3	1			
11				2			1	1		
10			1	2		1	1	1		2
9			1	1				1		
8				2	1	1		1		
7				1		1	1	2		
6				2						
5			1	1	3	1				
4				3		2				
3					1					
2	1	1	1	1						
1			1							
0	2	2	2							

not belonging to a single inbred strain. Animals suckling three young may or may not have a prolonged gestation, but all those suckling more than three exhibit prolongations of from two to sixteen days. Statistical examination of these data for animals suckling three or more young shows that a straight regression line of the form:

$$y = 0.84 + 3.94x$$

can be fitted (where y = the prolongation in days and x = the number of young suckled). Testing by means of the table of t (Fisher, 1930) with $t = 3.2$ and $n = 59$ the value of P is found to be below 0.01 and the regression must therefore be regarded as significant. Although a direct relation therefore exists between the number of young suckled above three and the duration of gestation, it does not approximate to the one day for each young suckled, as stated by Daniel (1910), and the individual variation exhibited is very wide.

Similar data for the albino rat, compiled from the records of Lataste (1887), King (1913), and Hain (1934), are given in Table IV. Since in this species the normal gestation period varies from twenty-one to twenty-three days, the prolongation was calculated by subtracting 22, the mean gestation period of nonsuckling females. Therefore, in Table IV, prolongations of one day cannot be considered significant.

the uterine lumen is prolonged by lactation, the growth of the corpora lutea is arrested also. So far as we are aware these data provide the only information available regarding the growth of the corpora lutea during gestation prolonged by lactation.

The researches summarized above amply confirm Lataste's original statement that gestation may be prolonged during lactation in the small rodents and show that a similar prolongation occurs in the shrews also. It is only in the rat and the mouse that sufficient records are available to warrant any conclusions being drawn regarding the relation, if any, between the number of young suckled or the number of embryos in the uterus and the duration of the prolonged gestation. Examination of these records provides no evidence that the number of embryos in the uterus has any influence on the duration of gestation. Moreover a priori such influence seems improbable since the prolongation is due to delayed implantation and would therefore have to be exerted by the embryos while still in the blastocyst stage free in the uterine lumen. This suggestion need not be considered further unless evidence is forthcoming in support of it. The possibility of a relation between the number of young suckled and the duration of gestation cannot be disposed of so easily. Lataste observed that gestation is not prolonged in the mouse unless more than two young are suckled, and that in the rat it was not prolonged when three young were suckled. He suggested that the minimum number of young necessary to cause prolongation may vary in different species. Subsequent researches confirm this conclusion so far as the rat and mouse are concerned. Daniel's data, although too meager to be conclusive, suggest that the duration of gestation may be directly proportional to the number of young suckled in the mouse; a conclusion which he attempted to formulate as a general law. Although all subsequent workers failed to confirm Daniel's conclusions on the basis of their individual results, examination of all the records available, compiled from several sources, seems desirable before arriving at a definite conclusion. The data given in Table III show the prolongations in days of 67 pregnancies in mice suckling litters of known size. These have been extracted from the papers referred to by Lataste (1887), Daniel (1910), Kirkham (1916 and 1918), and Mirskaia and Crew (1931). Only records of completed pregnancies or of animals killed after the embryos had become implanted, when the delay in implantation could be estimated accurately by comparison with embryos of nonsuckling females, have been employed. In calculating the prolongation twenty days has been taken as the normal gestation period, except in the case of the records of Mirskaia and Crew who employed a strain in which nineteen days was the normal.

we possess all the information necessary for its solution. It is obvious that the inhibition must be exerted, directly or indirectly, on the uterine endometrium or on the blastocysts or on both simultaneously.

The postestrous changes in the pregnant or pseudopregnant animal result in a progestational condition of the uterine endometrium which is invariably accompanied by sensitivity to mechanical stimuli. This was first experimentally demonstrated by Loeb (1908), who found that operative injury of the sensitive endometrium of the guinea pig resulted in the production at the site of injury of placentomas which resembled histologically the maternal placental tissues. Later Frank (1911) ascertained that a similar sensitivity exists in the rat and that in this animal placentomas could be produced experimentally during lactation, a discovery which was subsequently corroborated by Corner and Warren (1919) and by Long and Evans (1922). Although in the pseudopregnant rat, the sensitivity is at a maximum about the fourth day after estrus and has disappeared before the onset of the next estrus, the last named authors showed that it persists during lactation from the fourth to the sixteenth day *postpartum*. A similar sensitivity of the uterine endometrium in the lactating mouse was demonstrated by Parkes (1929).

It is well known that the sensitization of the endometrium and the other progestational changes in the uterus are effected by the action of the luteal hormone progesterone. Complete sensitization of the uterus can be produced experimentally by injection of this hormone, provided that, if the animals are immature or have been ovariectomized a considerable time previously, an initial sensitizing dose of estrin is administered some time before the progesterone.

Another function of the corpus luteum, which may or may not be independent of the progestational effect, is that of inhibition of estrus during either pregnancy or lactation. Estrus does not recur, after the *postpartum* estrus, during lactation in either the rat or the mouse, provided that a litter of normal size is being suckled. Estrus reappears in the suckling mouse about twenty-five days after the *postpartum* estrus (Parkes, 1926a) and in the suckling rat from twenty-five to forty days (Long and Evans, 1922). Mice suckling less than three young exhibit no such postponement of estrus, which then recurs at normal intervals during lactation (Parkes, 1926a). Estrous symptoms can be experimentally induced during lactation in mice suckling three or more young by the injection of the hormone estrin but the minimum amount of hormone necessary increases directly with the number of young suckled (Parkes and Bellerby, 1927). This phenomenon of inhibition of estrus during lactation in the mouse, appearing only when more than two young are suckled and exhibiting an intensity proportional to the number suckled has a curious, perhaps significant, resemblance to the phenomenon of prolonged gestation during lacta-

It is apparent that the gestation period in the rat may or may not be prolonged when three, four, or five young are suckled but that it is invariably prolonged when more than five young are suckled. The rat therefore differs from the mouse in the minimum number of young necessary to ensure prolongation. Moreover it can be seen from a glance at Table IV that a correlation exists between the number of young suckled and the duration of gestation. Probably the fact that almost all the data are derived from animals belonging to the inbred

TABLE IV

PROLONGATION IN DAYS	NUMBER OF YOUNG SUCKLED									
	3	4	5	6	7	8	9	10	11	
14								1		
13							1		1	
12							1		1	
11									1	
10										
9							1			
8						1		1		
7			1		1	1				
6		1			1	1				
5	1	1		1		1		1		
4	1			3						
3		2	1		2					
2	1	1	1							
1	2	2	3							
0	4	2	2							

Wistar Institute strain of rats accounts for the greater uniformity of the results as compared with the data on the mice, which were drawn from animals derived from many different sources. The linear regression line derived from Table IV is of the form:

$$y = 1.33x - 3.43.$$

It is clearly established that when lactation and gestation occur simultaneously, following the *postpartum* estrus, the duration of gestation is prolonged, provided that the number of young suckled exceeds a minimum which is characteristic for each species. The prolongation tends to be directly proportional to the number of young suckled but the individual variation is wide. This prolongation is due to delay in the implantation of the blastocysts in the uterine mucosa and an arrest in their development and is accompanied, in at least one species (bank vole), by an arrest in the development of the corpora lutea. When lactation is terminated by the removal of the young during the phase of arrest implantation follows rapidly.

The elucidation of the mechanism by which lactation brings about a temporary inhibition of implantation presents a difficult problem. Yet many lines of evidence converge upon it and it may well be that

passing from the fallopian tube into the uterus before implantation occurs. Implantation in the shrews, on the other hand, is of the central type in which the blastocyst, after reaching the uterus, enlarges considerably and, by distending the uterine lumen, becomes lodged in a spherical chamber. This chamber is of much greater diameter than the rest of the uterine lumen and opens freely into it. It is only after the formation of this chamber that the embryonic trophoblast becomes attached to the uterine epithelium with which it is in contact. Thus, while the blastocyst of the mouse undergoes little further development after reaching the uterus before implantation occurs, that of the shrew increases in size from 70 to 100 μ in diameter up to 800 to 1,000 μ before the zona pellucida disappears and the trophoblast becomes attached to the endometrium. Since the unimplanted blastocysts in the majority of parous shrews recorded above were of small or intermediate size, the arrest in their development during lactation must have taken place before they had attained the necessary size to become implanted. This suggests a positive inhibition of the blastocysts themselves, as distinct from an arrest in development occasioned by a failure on the part of the endometrium to react at the appropriate time and so provide the environment necessary for their further development.

The only suggestion that has been advanced as to how lactation could affect the embryos is that it lessens their food supply and so retards their development (King, 1913), but this was advanced before Kirkham had demonstrated that the arrest was prior to implantation. The intensity of mammary activity, in forms in which the milk secreted cannot be measured directly, can be estimated from the weight increments of the young during the period when they are entirely dependent on the mother for their nutrition. Parkes (1926b) has provided data of the average daily increments of young mice according to the size of litter suckled which admit of such an estimate. These data show that the daily weight increments rise at first to a peak between the fourth and eighth days *postpartum*, attained on an average for all litters on the seventh day, and thereafter fall off until

TABLE V

SIZE OF LITTER	NUMBER OF LITTERS OBSERVED	AVERAGE TOTAL INCREMENT DURING FIRST 15 DAYS GRAMS
1	1	12.2
2	2	14.5
3	5	14.82
4	7	19.08
5	9	19.7
6	8	21.42
7	15	24.57
8	12	25.52
9	5	25.56
10	2	24.5

tion. Parkes and Bellerby (1927) showed further that the inhibitory effect of lactation on estrus is exerted via the ovaries, and hence presumably by the corpora lutea, for mice ovariectomized early in lactation required only small amounts of estrin to induce estrous symptoms in them, irrespective of the size of litter suckled.

These considerations lead to the conclusion that the hormone progesterone, secreted by the corpora lutea, induces the progestational changes in the uterus and an appropriately sensitive condition of the endometrium for implantation to take place during lactation. Moreover the activity of the corpora lutea, so far as inhibition of estrus is concerned, actually increases with the number of young suckled. Since the ability of the endometrium to react to suitable stimuli by the production of maternal placental tissues during lactation in both the rat and the mouse must be admitted, the theory that delayed implantation is due to inactivation of the uterus is clearly invalidated, whether caused by loss of surplus nourishment through the mammary glands, as suggested by Kirkham (1916), or by insufficiency of luteal hormone for implantation and lactation to take place simultaneously, as suggested by Mirskaia and Crew (1931), or by any other means. Indeed Mirskaia's and Crew's theory must, in any case, be discarded since, as has been pointed out by Hain (1934), lactation can continue after the ovaries have been removed experimentally.

Since the corpora lutea are able to perform both the progestational and estrus-inhibitory functions in nonpregnant lactating rats and mice, it follows that the second growth phase in their development during pregnancy, which has been observed in mice (Deanesly, 1930) and which is delayed until implantation occurs in lactating bank voles, is not essential for the performance of these functions. It is probable that this second growth phase is stimulated by the process of implantation and that it is in the nature of a preparation for the luteal activity during the placental phase of gestation, since it occurs only during pregnancy.

The alternative theory that the delayed implantation is brought about by inhibition of the blastocysts remains. It is, at first sight, more difficult to conceive how this could be effected, since the blastocysts are free in the uterine lumen and have no organic connection with the parent. Yet, by a process of elimination, it appears the more probable explanation. The occurrence of delay in implantation during lactation both in small rodents and in shrews is significant in this connection, for the method of implantation differs widely in the two cases. Implantation in the mouse and its allies is of the excentric type, in which the blastocyst, while still very small, becomes lodged in a pit or depression in the endometrium which closes over it and shuts it off from the rest of the uterine lumen. Consequently the blastocyst undergoes comparatively little further development after

IDENTIFICATION AND SIGNIFICANCE OF SPIROCHETES IN THE PLACENTA

A REPORT OF 105 CASES WITH POSITIVE FINDINGS

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THE difficulty in the diagnosis of syphilis in pregnancy is not fully appreciated by the general practitioner. There is no entirely satisfactory test. It is exceptional for the blood of a newborn syphilitic baby to give a positive serologic reaction; and most syphilitic babies born at full term show no gross syphilitic lesions. The placenta of the full-term syphilitic baby is usually normal in appearance; the classical description in textbooks is rarely found, and when found is generally due to prematurity.

Two facts stand out prominently in the diagnosis of syphilis in pregnant women. First, in any woman syphilitic infection commonly occurs with no signs of primary chancre, rash or mucous patches, and second, the supervention of pregnancy seems to attenuate this infection.

Stokes¹ refers to the "suppressing effect of pregnancy" as placing syphilis in women in a field by itself, and states that the infection is to some extent inhibited by the pregnancy. Moore² says: "If infection occurs early in pregnancy, the usual early manifestations of syphilis are much milder than if she is infected independently of pregnancy. Many fail to develop any of the usual early lesions of syphilis." Halbrecht³ states: "We cannot rely on the Wassermann test in cases of hereditary syphilis, and it is most probable that fetal malformations represent forms of hereditary syphilis in the second and third generation." An illustration of the attenuation of syphilis is seen in the infrequency of complications of the nervous system following such cases. Zabriski⁵ states that women who undergo several pregnancies are less liable to neurosyphilitic lesions than primiparas or sterile women. He suggests that there may be some immunizing power in the cholesteremia that accompanies pregnancy. Others have attributed the diminished virulence to the effect of iodine from the hyperactive thyroid. Brown, quoted by Zabriski,⁶ has shown that extirpation of the thyroid in rabbits has a definite effect on the rapidity of development of primary and secondary lesions of syphilis. Routh⁷ suggests an antispirochetal action of "placental ferments" or "synectial toxins" that break up the spirals into granules and diminish their virulence.

As a result of attenuation—or some other factor—the Wassermann reaction is commonly negative in the syphilitic woman who is pregnant.

Guéniot⁸ reported before the French Academie de Medecine in 1934, 1,119 cases of pregnancy where the clinical histories were such as to justify a suspicion of syphilis. In only 3.75 per cent was the Wassermann positive. "It seems," he states, "as though there were in pregnancy a factor which attenuates and some-

the young begin to eat solid food about the fifteenth day. Thus mammary activity reaches a maximum about the time when the embryos, of a pregnancy originating at the *postpartum* estrus, would be implanting if their development were not arrested. Further, as might be expected, the intensity of mammary activity is proportional to the size of litter up to seven or eight but shows no further increase with larger litters. This is shown by the data of the average total increments of litters of 1 to 10 during the first fifteen days given in Table V.

Thus, if the drain on the maternal organism through milk secretion were the cause of prolonged gestation, the fact that it is at a maximum at the time when implantation would otherwise occur and decreases thereafter and is proportional to the number of young normally suckled, would account for many of the phenomena observed. Yet that it could inhibit the development of the blastocysts prior to implantation seems impossible, since, owing to their small size, their nutritional requirements could impose only an infinitesimal drain upon the parent organism. Moreover prolonged gestation occurs when only 3 to 6 young are suckled, yet the maximum activity of the mammary glands is not attained when less than seven young are suckled.

We are, therefore, forced to the conclusion that the explanation of the problem of how lactation brings about prolonged gestation is yet to be found. The evidence available appears to us to point to an inhibitory effect on the blastocysts themselves, exerted otherwise than through lack of nutriment, rather than to an effect on the uterine endometrium. Moreover, since the blastocysts are at this time free in the uterine lumen, without any organic connection with the parent, it would appear that this inhibition must be exerted through the medium of some substance secreted into the uterine lumen. It may be that this is a growth-stimulating substance, like that known to occur in certain embryonic tissue extracts, but of this there is at present no direct evidence.

I am indebted to my colleagues, Mr. L. H. Jackson and Dr. W. G. Ellis, for reading the manuscript of this paper and making many useful suggestions.

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search in the placenta may readily fail to reveal spirochetes which are actually present. That eggs are not found lying about the barnyard is no proof that they are absent from the nests in the henhouse.

It has seemed to us that a more systematic method or search in the probable localities might give a higher percentage of positive findings. Boyd¹⁵ states: "In congenital syphilis the primary lesion is in the placenta. There is, therefore, no primary stage in the child." That is to say, the primary focus being located in the placenta, it is not to be expected that there will be a widely disseminated lesion, but rather that there will be one or more sharply localized foci.

In the Obstetrical Department of the American University of Beirut, we have not felt justified with burdening our laboratories with routine Levaditi impregnation for all delivery cases in the hospital. We have contented ourselves with such examinations only in special cases. In cases of suspicious history, of positive serum reaction, of stillbirths, of prematurity, of placenta previa, of abortions, or of cesarean section, the examination has been made routine. In other cases where there is no suspicion of syphilis, the placentas are labelled and stored in a large jar of 5 per cent formalin until the baby is discharged from the hospital. In cases of neonatal death, or of any abnormality or lesion in the baby, the placenta is sent to the laboratory for examination by the Levaditi method.

In this way 145 placentas were chosen for examination from a total of 667 deliveries in the hospital during the two years, 1934 and 1935. In these 145 placentas, spirochetes were demonstrated in 105 cases, an apparent incidence of syphilis in the total number of pregnancies of 15.7 per cent. Among these 105 cases of positive findings were those who came to the hospital because of complications which had resulted from the presence of syphilis, such as abortions, stillbirths, polyhydramnios, and premature labor. For this reason the incidence of syphilis in the hospital is greater than it would be in cases of pregnancy delivered outside the hospital.

The modification of the silver impregnation method of search for spirochetes in the placenta consists in a more discriminating choice of sections and a more systematically directed hunt in the sections for the nests of spirochetes.

THE TECHNIC

The fresh placenta is placed in a flat jar containing 10 per cent neutral solution of formalin for twenty-four hours. Then it is cut through its longest diameter and a ribbon half a centimeter in thickness is removed. This is cut into pieces 3 or 4 cm. in length and allowed to fix in a 10 per cent neutral solution of formalin for three weeks or more, the longer the better. Twin blocks from each of these pieces are cut, one for ordinary paraffin inclusion, and the other, for silver impregnation. Sections from each of the paraffin blocks are stained with eosin and hematoxylin.

times renders negative the Bordet-Wassermann reaction.' Other French authors have reported similar low percentages: Nobécourt⁹ reported 18 per cent; Brindeau 9.6 per cent. Halbrecht⁴ points out that antisyphilitic treatment may result in a negative Wassermann reaction even though the spirochetes are still present in the system. For this reason antisyphilitic treatment should always be resumed during the course of every pregnancy where there has been a syphilitic history. In fact, it is doubtful if the system, once infected, is ever completely cleared of spirochetes. Warthin¹⁰ says: "I have never seen at necropsy a case of perfectly healed syphilis . . . there is no evidence pathologically that the case of syphilis ever becomes wholly free from spirochetes."

While it may be admitted that during the course of pregnancy the determination of syphilis is difficult, there is yet a prevailing belief that the birth of a healthy baby is a good indication that the child is free from syphilis. This is not true. The baby may look healthy; the placenta normal to gross appearance; the cord Wassermann negative; and yet the child may be afflicted with congenital syphilis. It is also a common belief that the placenta will tell the tale, if not to the naked eye, at least under the microscope. But the ground for this belief is now called in question.

Montgomery¹¹ says: "Those histologic changes which we have attributed to syphilis are due to nothing more than the immaturity of the placenta and the accumulation of edema." McCord¹³ commenting on Montgomery's article says: "Formerly I believed that there was a definite histologic appearance of the placenta that was a constant pattern for syphilis, but I no longer think that is true." Ingraham, Jr., and Kahler,¹⁴ in a masterly review of the literature on the subject, conclude: "The diagnosis of syphilis in the mother or her child after birth is no easy matter, if you would approximate a hundred per cent accuracy . . . nothing short of a demonstration of treponemas in the fetal circulation of the placenta is indicative of a positive diagnosis of syphilis in any one but the mother."

Since in the presence of syphilis characteristic lesions are not to be expected in the mother, in the child or in the placenta, and since the serum reaction in such cases for both mother and child is commonly negative, the identification of spirochetes that may be present in the placenta becomes a matter of prime importance.

The introduction in 1906 of the Levaditi method of silver impregnation in the exploration of tissue for spirochetes has been of the utmost service. But in the examination of the placenta the results have been disappointing. The long and tedious process involved in the search for the spirochetes in the placenta has been rewarded only too frequently by negative findings in cases where the clinical symptoms clearly indicated the presence of syphilis. Montgomery¹² speaking of the *Treponema pallidum* says: "Their discovery in the placental substance happens so infrequently as to be of negligible value pathologically." A possible reason for this infrequency lies in the fact that the spirochetes are not equally distributed throughout the placenta, but are commonly clustered together in small foci, with large areas of the placenta totally free from their presence. Thus an indiscriminating



Fig. 1.



Fig. 2.

Fig. 1.—Normal blood vessel of the placenta. ($\times 200$ mag.)

Fig. 2.—Normal thickening of blood vessel often found in full-term placenta. ($\times 200$ mag.)

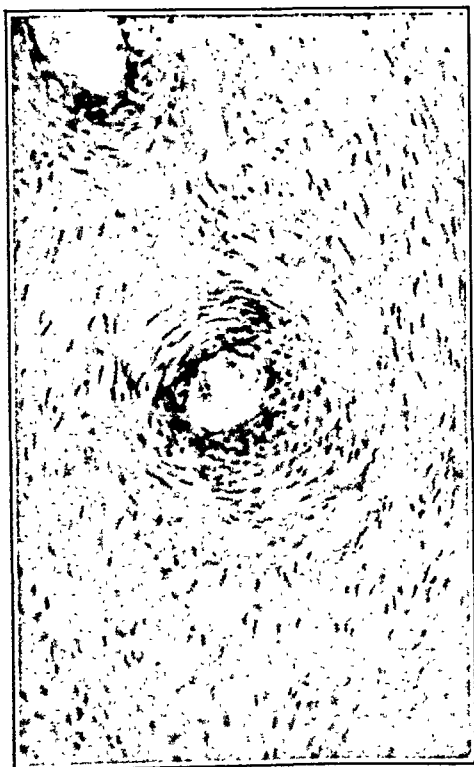


Fig. 3.



Fig. 4.

Fig. 3.—Case 86. Table VI. Warthin's criterion.—Blood vessel showing peri- and endarteritis with lymphocytic and plasma cell infiltration. ($\times 200$ mag.)

Fig. 4.—Same case as Fig. 3. ($\times 400$ mag.)

The silver impregnation method used is Nyka's modification of Levaditi's silver technic:¹⁶

After fixation for at least three weeks, proceed as follows:

1. Wash in 96 per cent ethyl alcohol for twenty-four hours.
2. Wash repeatedly in distilled water for twenty-four hours, changing the water often.
3. Impregnate for two to four days in 1.75 per cent silver nitrate solution in bidistilled water at 37° C.
4. Wash rapidly in bidistilled water.
5. Reduce for twenty-four hours in the following solution:

Pyrogallie acid 4 per cent	90 c.c.
Pyridine	17 c.c.

 Acetone drop by drop to dissolve the precipitate.
6. Wash rapidly in bidistilled water.
7. Dehydrate in alcohol.
8. Clear in xylol.
9. Include in paraffin.
10. Cut sections, mount, and after clearing in xylol, mount in Canada balsam.

In the eosin and hematoxylin sections the Warthin criterion is looked for, i.e., blood vessels showing mild peri- and endarteritis, with plasma cells and lymphocytes in the form of mild perivascular infiltration. The caliber of the blood vessel is strikingly narrower than normal on account of this inflammatory process (Figs. 1, 3, and 4). Spirochetes cannot be identified by the eosin and hematoxylin stain, but the presence of the Warthin criterion suggests the likelihood of finding the spirochetes in the Levaditi twin section. Infarction, hyalinization, deposition of lime salts, or ordinary thickening of the blood vessels (Fig. 2) does not indicate or suggest the presence of spirochetes.

In the silver impregnated twin sections, foci are looked for under the low power which take a pale yellow stain and are surrounded by a dark powdery deposit (Fig. 5). In these and especially around them the spirochetes are usually found (Fig. 6). These foci are generally located near the amniotic surface of the placenta, but may be found in other sites. They have no direct relation to the vascular lesions already described in the eosin and hematoxylin sections but may be found in their vicinity. Their appearance and topography convey to the careful observer the impression of miliary gummas. We have not been able to find spirochetes in the placental infarcts.

Under the oil immersion the spirochetes were numerous and easy to find in some cases (Figs. 6 and 7), while in others they were very few and surrounded and covered by a blackish brown precipitate, possibly the remnants of broken spirochetes.¹⁷ It is, therefore, necessary to examine sections from all the blocks prepared before pronouncing a placenta free. Four out of five blocks examined might be negative while a fifth might show spirochetes in abundance.

While we have no proof as to the exact nature of these spirochetes, the forms seen in the Levaditi silver sections cannot be differentiated morphologically from the *Treponema pallidum* as to length, thickness, number of coils and general appearance. The large percentage of agreement between the clinical evidence of syphilis and the laboratory findings of spirochetes in the placenta, as we shall see later, is a strong indication that they are, at least for the most part, the *Treponema pallidum* of syphilis. These findings have been corroborated by E. W.

Dennis, Professor of Parasitology, and D. Berberian, Adjunct Professor of Parasitology, in the medical school of our institution, to both of whom we are indebted for helpful cooperation and suggestions.

It is probable that the majority of spirochetes seen in our cases are syphilitic, but it is realized that our study is still far from complete. Examination of scrapings of the wall of the umbilical vein by the dark-field has been done in a few of our cases, with unsatisfactory results. More exact determination of the variety of spirochetes encountered might be obtained with inoculation into the testes of the rabbit. This has not been done on account of lack of funds. No check up of possible syphilitic perichondritis of the epiphysis of long bones by the roentgen ray has been done by us on living babies. However, twenty cases of stillbirths in this series were autopsied and in each case the bones were free from evidence of osteochondritis. At the Johns Hopkins Hospital 25 per cent of premature babies examined by x-ray, showed signs of syphilis of bone.¹⁸ On the other hand Olsen¹⁹ has reported that of 55 viable healthy children of syphilitic mothers in the Rigs Hospital, Stockholm, who were examined by the x-ray on the second and third days after birth, only one showed osteochondritis.

We feel that while this preliminary report is not complete, there is enough evidence to stimulate further research on this vital problem.

In the 105 cases the average age was 27.3 years, the patients ranging in age from sixteen to fifty-nine years. In 21 per cent of the patients the placenta examined was from the first pregnancy.

A STUDY OF 105 CASES OF POSITIVE FINDINGS OF SPIROCHETES IN THE PLACENTA

TABLE I. PRESENT DELIVERY		TABLE II. CONDITION OF FETUS	
Normal delivery	56	Normal	64
Forceps	14	Stillborn	32
Embryotomy	3	Neonatal death	9
Cesarean section	11		—
Version	3	Total	105
Premature	18	Of these 18 presented abnormalities	
Total	105		
The following conditions were found:			
Placenta previa	9		
Adherent placenta	7		
Polyhydramnios	11		
TABLE III. WEIGHT OF FETUS		TABLE IV. PAST HISTORY	
2,000 gm. and under	4	Number of primigravidas	22
2,000-2,500 gm.	9	Number who had had at least one normal child	65
2,500-3,000 gm.	19	Number who had had at least one abortion	51
3,000-3,500 gm.	28	Number who had had at least one stillbirth	27
3,500 gm. and over	16	Number who had had at least one neonatal death	5
Weight not recorded—cases of maceration, embryotomy, etc.	29	Number who had had at least one premature birth	3
Total	105		

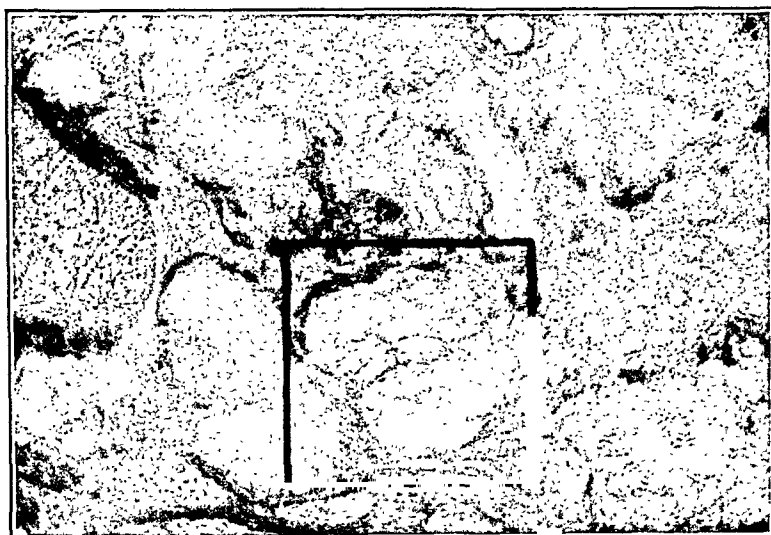


Fig. 5.—Case 86. Levaditi silver impregnation. Square indicates the gummatoid lesion in which the spirochetes are found. ($\times 200$ mag.)



Fig. 6.—Same as Fig. 5. Oil immersion showing spirochetes and dark brownish black granules. ($\times 900$ mag.)

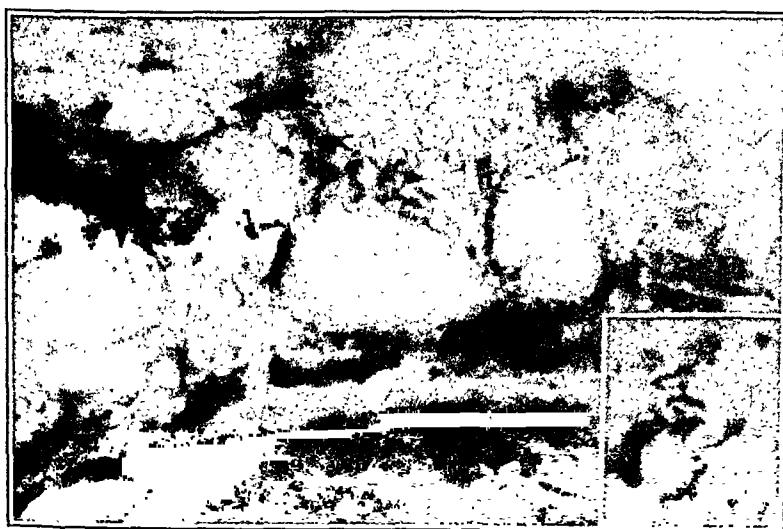


Fig. 7.—Case 7. Extensive infiltration with spirochetes. ($\times 900$ mag.) *Inset.* To show coils of individual spirochete. ($\times 1200$ mag.)

3. It is probable that the character of the invasion is determined by the stage of the disease in the mother, whether it is quiescent or in active stage.

4. The relation of the time of the invasion of the fetus to the vulnerable stages of development of its vital organs.

5. The presence of other complicating lesions such as nephritis.

If the infection is from a mild strain, or the disease is in a quiescent stage, one may anticipate the advent of an apparently normal child, though spirochetes are present in the placenta.

CASE 23.—(Hospital No. 21230.) Patient aged 23, married eight years. Four healthy full-term babies. No abortions. In the last pregnancy the mother's blood gave a two-plus Wassermann; the cord blood was negative. In the present pregnancy only had the mother received antisyphilitic treatment. The placenta showed numerous spirochetes in clumps.

CASE 83.—(Hospital No. 24195.) Patient aged thirty-seven, married twenty years. Five normal full-term children. One abortion. The last delivery was a placenta previa with adherent placenta. The cord blood was negative. Spirochetes were found in the placenta. Had it not been for the presence of a placenta previa there would have been no examination made of the placenta.

CASE 85.—(Hospital No. 24490.) Patient, aged thirty-five, married eighteen years. Has had seven normal full-term deliveries and no abortions. Eleven years previously she had an attack of eclampsia. In the present pregnancy she had an albuminuria of 4-plus, and her blood pressure rose to 210/120. Serodiagnosis of the maternal blood was negative. She aborted a seven months' macerated fetus which had been two months dead in utero. The placenta showed typical spirochetes. Had it not been for the complicating nephritis, the probability is that the child would have been born alive at term.

On the other hand the syphilitic infection may be of such a virulence that pregnancies end in repeated disaster. In one of the cases in this series spirochetes were demonstrated in the placenta of an abortion of four months.

CASE 67.—(Hospital No. 23536.) Patient aged twenty-six, married ten years. Had four premature stillbirths at approximately eight months. Antisyphilitic treatment was then instituted and she gave birth successively to three healthy children at term. The cord blood was negative; nevertheless, the placenta of the last case showed the presence of spirochetes in a few foci only.

Other syphilitic mothers alternate between disaster and success in their pregnancies. We may suppose that in such cases the varying results of pregnancies are determined by the different factors already enumerated.

CASE 91.—(Hospital No. 14562.) Patient aged thirty, married fourteen years. Interspersed with 5 normal full-term children there were one stillbirth, one neonatal death, and one fetus dead at four months. In the last pregnancy only was the patient given a quite inadequate antisyphilitic treatment. The mother's blood gave four-plus Wassermann. The pregnancy was successful in delivering a full-term, apparently normal child. Kahn precipitation test showed four-plus for the cord blood. The placenta showed spirochetes.

NORMAL CHILDREN FROM SYPHILITIC MOTHERS

Half of the patients gave a history of at least one previous abortion and one-fourth of the patients a history of repeated abortions. While this figure may seem high, it should be borne in mind that the history of repeated abortions was one of the factors that determined the selection of the placenta for examination.

The past and present history of these 105 patients includes a total of 558 pregnancies. The history of previous pregnancies gave a record of delivery of full-term living children in 61 per cent of the cases, and in the present series of 105 deliveries in which the spirochetes were found in the placenta, no less than 63 per cent were children to all appearances perfectly healthy. Thus we see that the presence of spirochetes in the placenta is perfectly consistent with a seemingly healthy baby.

Of these 558 pregnancies, 238 ended "disastrously" and 320 in apparently normal full-term babies. The "disastrous" pregnancies, as McCord terms them, were: 112 abortions; 48 stillbirths; 23 neonatal deaths; 37 premature labors; 18 full-term babies showing abnormalities. Of the 320 apparently normal children 15 were killed by accidents of birth: 4 placenta previa; 8 dystocia; 3 prolapse of the cord.

Of the 105 patients with the positive findings of spirochetes in the placenta, 30 patients had received antisyphilitic treatment of some sort either before or during the present pregnancy, and 75 patients received no antisyphilitic treatment. The 75 mothers who had not received any treatment gave a history, including the last delivery, of having produced 231 apparently healthy babies and of 160 "disastrous" pregnancies: 74 abortions, 29 stillbirths, 17 neonatal deaths, 22 premature labors, and 18 children showing abnormalities.

Thus it will be seen that the chance of a successful pregnancy in an untreated case of syphilis is only a trifle less than 3 out of 5. The possibility is realized that with some of these mothers syphilis may have been acquired after the birth of the earlier children, but such instances are very few and in the majority of cases the seemingly healthy children are the product of later pregnancies.

VARIED RESULTS FROM THE INFECTION OF THE PLACENTA

While the above proportion of 3 successful pregnancies out of 5 may be true as the average for those 75 cases, it does not hold true for any one individual case. A number of factors may be assumed to influence the course of pregnancy in a syphilitic mother.

The course may vary with:

1. The virulence of the strain of spirochetes.
2. The character of the invasion, whether gradual or abrupt, as well as the massiveness of the infecting dose.

TABLE VI. FORTY-SIX PATIENTS WITH SUSPECTED SYPHILIS NOT RECEIVING ANY ANTISYPHILITIC TREATMENT

CASE	PAST HISTORY				SYNOLOGY	PRESENT DELIVERY			REMARKS
	ABORTION	PREMATURE	STILLBIRTH	NEONATAL DEATH		DEAD	NORMAL	ABNORMAL	
3	1	-	-	-	-	-	1	-	
4	-	1	-	-	-	1	-	-	Hydramnios
5	3	-	-	1	-	1	1	-	Twins, one neonatal death, oligo-hydramnios
6	3	-	-	-	-	-	1	-	
9	-	-	-	-	0	-	-	1	Talipes
10	3	-	-	-	+	1	-	-	
13	1	-	-	-	+	1	-	-	Macerated fetus
14	1	-	1	-	0	1	-	-	Large overtime fetus
15	3	-	-	-	-	1	-	-	Anemia, nephrosis, cesarean section
16	1	-	1	-	-	-	-	1	Macular rash on baby's trunk
17	-	-	-	-	-	1	-	-	Anencephalus
18	3	-	-	-	-	-	-	1	Cleft palate
21	2	-	3	-	-	1	-	1	Twins, one dead seven mo. Genu varum
24	2	-	1	-	-	1	-	-	Intrauterine asphyxia
26	1	-	-	3	-	-	1	1	Twins, one normal, one amyotonia
28	1	-	-	-	0	1	1	-	Twins, one normal, one stillbirth
32	1	-	-	-	0	-	-	1	Full term but very small
33	1	-	-	-	0	1	-	-	Intrauterine asphyxia
36	2	-	-	-	-	-	1	-	Albuminuria of pregnancy
37	-	-	-	-	0	-	-	1	Skin lesions, exfoliation
40	2	-	-	-	0	-	1	-	History of one hydatiform mole
41	3	-	-	-	-	-	-	1	Mongolian idiocy
45	12	-	1	-	0	-	-	1	Clubbed feet
46	3	-	1	-	+	-	1	-	Developed melena
47	-	-	-	-	++++	-	1	-	Cord Wassermann strongly positive
49	-	-	2	-	-	1	-	-	Macerated fetus
50	1	-	-	-	-	1	-	-	Prolapse of cord
51	3	-	-	-	0	1	-	-	Abortion at 4 months
52	1	-	1	-	++++	-	1	-	Cord Wassermann ++++
53	-	-	1	-	0	1	-	-	Eclampsia, intrauterine asphyxia
54	1	-	1	1	++++	1	-	-	Polyhydramnios cord ++++
58	1	-	-	-	-	1	-	-	Premature, died third day
60	-	-	1	-	0	1	-	-	Macerated
63	-	-	-	-	-	-	-	1	Osteogenesis imperfecta
64	-	-	1	-	-	1	-	-	Left tentorial tear
70	-	-	-	3	-	-	1	-	Died third day, acute purulent colitis
79	1	-	-	-	-	1	-	-	Macerated, father - - - - Wassermann
80	-	-	-	-	-	-	1	-	History of positive Wassermann
81	1	-	-	-	0	1	-	-	Bleeding 40 days before abortion
86	-	-	1	-	-	-	1	-	Cesarean for narrow pelvis
87	-	-	-	-	-	-	-	1	Cretinlike, mother enlarged thyroid
89	3	-	-	-	-	-	1	-	Prolapse of cord
92	1	-	-	-	-	1	-	-	Placenta previa, premature 8 mo.
97	4	-	-	-	-	-	1	-	Polyhydramnios
98	-	-	-	-	+	-	1	-	Manual extraction of placenta
101	1	-	-	-	0	1	-	-	Central placenta previa 8 mo.
46	63	1	16	10	25 neg. 8 pos. 13 not done	24	15	11	

CASE 97.—(Hospital No. 24880.) Patient aged twenty-six, married fifteen years. She has had five apparently normal full-term babies, of whom three are now alive. Has had four abortions. Has had no antisyphilitic treatment. In the present pregnancy the serum reaction for both maternal and cord blood was negative. Patient was delivered of a cyanosed eight-month baby. There was polyhydramnios estimated at five liters. The baby lived. A few spirochetes were found in the placenta.

RESULT OF ANTISYPHILITIC TREATMENT

Our records show that in pregnancy with syphilis thorough treatment may be expected to result in successful outcome of the pregnancy in better than 90 per cent of the cases. They also show that an apparently healthy child is frequently born of a syphilitic mother who has

TABLE V. RESULTS OF 30 TREATED AND 75 UNTREATED CASES

	NO. OF CASES	NO. OF PREG- NANCIES	AP- PARENTLY NORMAL	DIS- ASTROUS
Suspected of syphilis and treated	30	167	89	78
Suspected of syphilis and untreated	46	307	163	144
Syphilis suspected during or after delivery; untreated	29	84	68	16
Total	105	558	320	238

NOTE: This table, superficially giving the impression that disastrous pregnancies were more common among the treated, is deceptive. It must be remembered that the patients that were treated were flagrantly syphilitic and were treated for the most part during the last pregnancy only. Tables VI and VII throw a better light on it.

had no treatment at all, and further, that even with thorough anti-syphilitic treatment, repeated at each pregnancy, the placenta of an apparently normal child is likely to show the presence of spirochetes.

CASE 20.—(Hospital No. 13136.) Patient aged twenty-seven, married twelve years. The first three children were stillborn at seven, eight, and nine months, respectively. Four years ago during her fourth pregnancy, her blood showed four-plus Wassermann. This time she delivered a full-term child that later died of diphtheria at the age of three. Serodiagnosis of the cord blood was negative. Three years ago after antisyphilitic treatment during her fifth pregnancy, she had another apparently healthy boy. Serodiagnosis of the cord blood was again negative. In the present pregnancy she was again given antisyphilitic treatment. The maternal blood gave negative Kolmer and Kahn reactions. She was delivered of eight-month twins, small, but apparently healthy. Kolmer and Kahn reactions from the cord blood were negative. Examination of the placenta by the Levaditi method showed abundant precipitate and a few spirochetes.

CASE 95.—(Hospital No. 4889.) Patient aged thirty-eight, married fourteen years. Husband gave history of primary chancre and of strongly positive Wassermann. There were three premature deliveries, two at eight and one at seven months, with neonatal death, and one stillbirth years ago. About six years ago she was given antisyphilitic treatment which has been repeated in each subsequent pregnancy, with the result of four successive apparently normal full-term children. In the last pregnancy the maternal and cord blood gave negative serum reactions. The placenta showed spirochetes in a few foci.

SEROLOGIC FINDINGS IN CASES OF POSITIVE FINDING OF SPIROCHETES
IN THE PLACENTA

Less than one-third of these cases gave any degree of positive serum reaction from the mother's blood, and these were all cases in which the spirochetes were demonstrated in the placenta. This is in accord with the statement of Gellhorn²⁰ that after five years of syphilis, whether treated or untreated, 60 per cent or more of the patients gave negative serologic tests.

TABLE VIII

	NEGATIVE	+	POSITIVE			TOTAL
			+	++	+++	
Maternal blood in 75 cases	54	12	2	1	6	21
Per cent for maternal blood	72	16½	2½	1½	8	28
Cord blood in 71 cases	64	2	1	1	3	7
Per cent for fetal blood	90	3½	1½	1½	4½	10

NOTE: In about half the cases the serum diagnosis was made by the Kolmer-Wassermann method as well as by the Kahn. In the others the Kahn alone was used, but wherever this was positive the Kolmer was also done. Usually the results of the two methods were the same. In 4 cases only the Kahn was positive and the Kolmer negative, and these were recorded as positive.

From the cord blood only 10 per cent of the cases gave positive reactions, and these only in cases where the mother's blood also gave a positive reaction. Where a positive reaction from the cord blood can be obtained in only 10 per cent of the cases in which the spirochetes are demonstrable in the placenta, the futility of reliance on the examination of the blood of the newborn is apparent. It is quite probable that fetal blood itself gives no positive Wassermann reaction and that the few instances where positive reactions are obtained occur only in those cases where the trauma of delivery has permitted a leakage of maternal blood through the placenta into the fetal circulation.²¹

THE RELATION BETWEEN THE CLINICAL DIAGNOSIS OF SYPHILIS AND THE
DEMONSTRATION OF THE SPIROCHETES IN THE PLACENTA

The clinical diagnosis of syphilis was judged by the presence of repeated abortions, stillbirths, or premature deliveries; by positive serodiagnosis; by previous history of syphilis; or by the presence of physical signs. The unsuspected cases include cases of single abortion, of placenta previa, of cesarean section, of stillbirths and of deformities

TABLE IX

CLINICAL DIAGNOSIS		SPIROCHETES PRESENT IN PLACENTA		
Total number of cases		Few	Moderate	Numerous
Syphilis probable	63	22	26	15
Syphilis questionable	13	3	8	2
Syphilis unsuspected before delivery	29	10	17	2
Total	105	35	51	19

TABLE VII. THIRTY PATIENTS WITH SUSPECTED SYPHILIS RECEIVING ANTISYPHILITIC TREATMENT DURING THE LAST PREGNANCY FOR THE MOST PART

CASE	PAST HISTORY				SEROLOGY	TREAT- MENT		PRESENT DELIVERY			REMARKS
	ABORTION	PREMATURE	STILLBIRTH	NEONATAL DEATH		PAST	PRESENT	DEAD	LIVING		
									NORMAL	ABNORMAL	
1	4	-	-	1	-	-	+	1	-	1	Twins, living had erythematous rash; dead transposition of viscera
2	4	-	-	-	++++	+	+	-	1	-	Mother bismuth line on gum
7	1	-	-	-	+++	-	+	-	1	-	
8	-	2	-	-	-	+	-	-	1	-	
11	1	-	-	-	-	-	+	-	1	-	
19	-	4	-	4	0	-	+	-	1	-	Baby had repeated attacks of cyanosis, atelectasis, recovered
20	-	3	3	-	-	+	+	-	2	-	Twins, healthy, 8 months
23	-	-	-	-	++	-	+	-	1	-	
27	-	-	1	-	-	-	+	-	1	-	Cesarean section
38	-	-	-	-	++++	+	+	-	1	-	
42	-	-	1	-	-	+	+	-	1	-	Father had positive serology
43	1	-	-	-	++++	-	+	-	1	-	Cord Wassermann +++
44	4	-	-	-	-	-	+	-	1	-	Premature at 8 months
55	3	1	1	-	-	-	+	-	1	-	
59	3	-	-	-	-	+	+	1	-	-	Abortion at fifth month
61	2	-	-	-	-	+	-	-	1	-	
67	1	-	4	-	0	+	-	-	1	-	
71	4	-	1	-	0	-	+	-	1	-	
74	1	-	2	-	+	+	+	-	1	-	Cesarean section
75	4	-	-	-	+	-	+	-	1	-	
76	2	-	-	-	-	+	+	-	1	-	
77	-	-	2	-	-	+	+	-	1	-	
78	-	2	-	-	-	+	-	-	1	-	
91	1	1	1	1	++++	-	+	-	1	-	Cord Kahn ++
93	2	-	-	-	+	+	+	-	1	-	
95	-	3	1	-	-	+	+	-	1	-	
96	3	-	-	-	-	+	+	-	1	-	
99	-	-	-	-	-	+	+	-	1	-	
103	-	-	3	-	-	+	-	-	1	-	Child lived 2 days. Bronchopneumonia
105	2	-	1	-	0	+	+	-	1	-	Cesarean section
30	43	16	21	6	17 neg. 9 pos. 4 not made			2	29	1	

NOTE: A synopsis of this and the previous table shows the benefit of anti-syphilitic treatment. In Table VI, of 46 untreated patients there were 50 babies (four twins), 24 dead and 26 living (16 being normal and 10 showing abnormalities). In Table VII of 30 treated patients there were 32 babies (two twins), 2 dead and 30 living (29 being normal and only one showing abnormality). Again note the higher percentage of serologically positive reactions among the treated cases than among the untreated, showing that the treated cases were the more strongly syphilitic.

CHRONIC UTERINE DISTENTION AND ITS RELATION TO THE END OF GESTATION*

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IN 1913, Dickinson and Smith published a paper² entitled, "The Treatment of Antelexion, Defective Function, and Sterility by Glass or Silver Stems." One of their concluding remarks contains the statement that insertion of stem pessaries into the cervical canal "may develop an infantile uterus, restore the organ of premature menopause or atrophy, and bring back superinvolution to a normal condition. Ovarian enlargement will take place *pari passu* with the uterine enlargement."

This observation, made when the nature and number of ovarian hormones was unknown, has remained unnoticed for nearly twenty-five years without attempt by physiologists to learn more of the effects of uterine distention upon reproductive functions. The present paper is a beginning, it is hoped, of what may prove to be recognition of the importance of uterine distention in certain phases of uterine function. At the same time, it may serve to reawaken the interest of the clinician in the possibilities of chronic distention in conjunction with attempts at modern ovarian hormone therapy.

I. HISTORICAL CONSIDERATIONS

Some importance has been attached in the past by clinicians to uterine distention. Thus the fact is well known that the size of a uterus in advanced ectopic pregnancy is smaller than is that of another uterus at a comparable stage of normal pregnancy. On the experimental side, Blair-Bell and Hick, in 1909, compared¹ the similarity of structure of the myometrium in the pregnant uterus before and after evacuation to the structure of the myometrium in experimentally produced hydrometria before and after emptying the uterus. Aside from this work which seems to have been little noticed in the intervening years, the question of the relation of uterine distention to uterine function has been generally neglected until recently.

In 1929, Knaus^{5a} showed that an occupied horn of a rabbit's uterus in unilateral pregnancy is significantly larger than the sterile horn in the same animal. In such a case, both uterine cornua are exposed to

*The experiments on the effects of graded uterine distention which are summarized and discussed together for the first time in this paper, were carried out with the aid of a grant of money to the writer from the Committee for Research in Problems of Sex, of the National Research Council. Acknowledgment to that Committee is gratefully made.

in the fetus. The histologic condition of the placenta was not taken into consideration in the composition of this table.

During the period in which the 105 cases with positive findings were under investigation, forty other cases were studied in which negative results were reported. In 11 of these the clinical history made a diagnosis of syphilis probable, but no spirochetes were found in the placenta. In the other 29 cases, where there was no presumption of syphilis, the findings were negative.

SUMMARY

1. The finding of spirochetes in the placenta in 105 cases is recorded.
2. Spirochetes can be found in the placenta of the syphilitic newborn in sufficient frequency to justify the search for them in suspicious cases.
3. The search should be made after Levaditi infiltration in portions of the placenta which give an indication of their presence by the presence of pale yellow foci surrounded by dark granular peripheries.
4. In 391 pregnancies from 75 syphilitic mothers who were untreated and with whom there were demonstrable spirochetes in the placenta of the last delivery, an apparently healthy baby was produced in three out of five pregnancies.
5. The fact that the newborn baby appears to be healthy does not indicate the absence of syphilis.
6. The successful termination of pregnancy after antisyphilitic treatment does not denote the absence of spirochetes from the placenta.
7. The histopathologic appearance of a placenta containing spirochetes is discussed.
8. Thorough antisyphilitic treatment, while it may not cause the disappearance of spirochetes from the placenta, is nonetheless indicated as it assures about 90 per cent apparently healthy full-term babies.

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tomized rabbits was established.¹² This curve shows that if a pellet is to be an adequate stimulus for growth it must be more than half the size of the undistended uterus yet less than twice its size. The largest growth responses are obtained when the uterus and pellet are of approximately equal sizes.

As a consequence of the establishment of these relationships in the absence of ovarian hormones, a base line was obtained to which the separate actions of estrin and progestin on the distention-growth response could be referred. Accordingly, two new sets of experiments were performed to evaluate quantitatively the effects of estrin and progestin respectively in uterine growth resulting from distention.

In one group of experiments⁹ estrin was given before and during the period in which the pellets were inserted. It was found that chronic uterine distention in these estrinized rabbits resulted in a reduction of the capacity of the uterus to grow. This reduced growth capacity of the tissues was more pronounced in the endometrium than in the myometrium and in both tissues the growth responses were much less than in the untreated, ovariectomized rabbit. This effect was explained on the basis of a diminished blood supply at the site of distention, resulting from the increased tonicity and contractility of the myometrium under the influence of estrin.

The second group of experiments¹⁰ was designed to show the effect of progestin upon the distention-growth response of the uterus. The results showed that in mature, ovariectomized rabbits treated with progestin, growth of the tissues about the pellets takes place. The form of the growth curve in these experiments is very similar to that obtained in untreated, ovariectomized rabbits. The limits of the curve are different, however, for it was found that if the pellets are to be an effective stimulus, they must be more than two-thirds the size of the undistended uterus (instead of half, as in untreated rabbits), yet less than four times the size of the undistended uterus (instead of twice the size, as in untreated rabbits). Optimal growth responses are obtained in progestin-treated rabbits when the pellets are about twice the size of the undistended uterus, in contrast to the untreated rabbits in which optimal growth is observed when the pellet and uterus are of equal size.

Briefly summarized, these results show that when progestin is acting upon the distended uterus, the degree of distention required to produce a given amount of growth must be appreciably greater than that required to have the same effect in untreated, ovariectomized rabbits. This fact has been ascribed to the decreased tonicity of the myometrium resulting from the action of progestin upon it. As a consequence, it appears that the increased distention is required to produce an appropriate degree of tension which is essential for the distention-growth response. As mentioned above in connection with the effects of estrin,

the same hormone environment. This observation has been confirmed on several recent occasions (rabbit, 3 and 7; cat, 6) and serves to extend to the rabbit (and cat) the older observation of the clinician with respect to the size of the uterus in ectopic pregnancy. Another advance in our appreciation of the rôle of distention alone (in contrast to the more complicated conditions associated with pregnancy) was made in 1929 by van Dyke and Gustavson¹⁴ when they observed that if rolled rubber dam is inserted into a uterine horn during pseudo-pregnancy, local uterine growth takes place at the site of distention. This observation, made in connection with experiments designed for another purpose, has escaped the notice of other investigators until now. Another finding which is comparable to that of van Dyke and Gustavson has been reported recently by Markee, Wells and Hinsey.⁷ These investigators noted that uterine growth takes place in a uterine horn distended with fluid secreted by its own endometrial glands. This observation differs from the earlier ones of Blair-Bell and Hick who stressed only the histologic features of experimental hydrometria in that this newer work established with quantitative measurements the fact that uterine enlargement occurred.

These considerations demonstrate that there is a local factor favoring uterine growth at a site of distention, but they do not show that this factor operates in the absence of ovarian hormones since the ovaries were present and functioning in each instance. Consequently, these experimental data do not constitute a confirmation of the earlier clinical work of Dickinson and Smith in whose observation uterine enlargement, ovarian enlargement, and even restoration of periodic bleeding resulted from uterine distention during a hypohormonic (amenorrhoeic) state. Experimental confirmation has lately been forthcoming as regards their observation pertaining to uterine enlargement, however. This has been obtained as a result of uterine distention in untreated, ovariectomized rabbits.¹²

II. EFFECTS OF GRADED UTERINE DISTENTION UNDER VARIOUS HORMONIC CONDITIONS

Experimental confirmation of the clinical observations of Dickinson and Smith was obtained in experiments of the following type. Suitable rabbits were ovariectomized and at the end of one week, paraffin pellets (melting point 56° C.) were inserted into the uterus per vaginam and anchored in place. Two weeks later these distention sites were taken, along with a segment of undistended, untouched uterus. With the aid of an appropriate technic,¹² the percentage increase (growth) of the various distention sites was determined. The extent of this growth was then correlated with the degree of distention (i.e., the intensity of stimulation) in each instance. As a result, the curve of uterine growth to graded degrees of distention in untreated, ovariect-

two the weights given for the single sterile horns, or by dividing by two the weights given for the gravid uterine horns. The former has been done in this paper. Such a procedure is permissible for two reasons. In the first place, Markee, Wells and Hinsey have shown that in a nonpregnant rabbit the sizes of the two uterine cornua are not appreciably different. In the second place, it is allowable because of the fact that Hammond quotes average weights for a number of cornua at the several stages of pregnancy studied, and he has used rabbits which "have been standardized as far as possible by using inbred strains which were selected for a definite size and fertility."

The data which are available, therefore, and are useful in the considerations which follow are: (1) the days of pregnancy; (2) the mass of the products of conception; (3) the mass of the gravid uterine tissues; (4) the mass of the sterile horn equivalent in each gravid

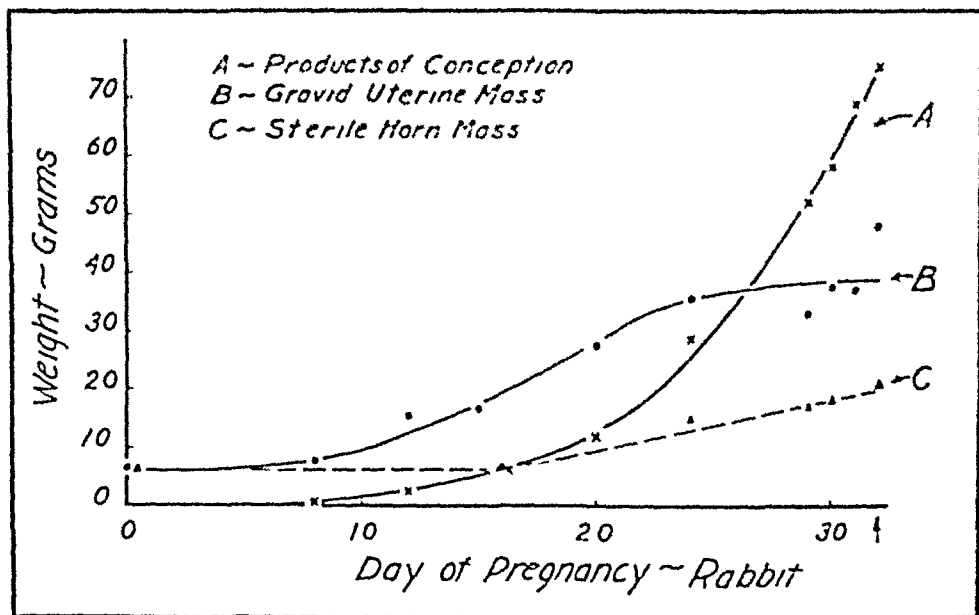


Fig. 1.—Chart showing growth during pregnancy of the products of conception (A), the gravid uterus (B), and of the sterile horn mass (C) calculated from unilateral pregnancies. Data from Hammond.

uterus; and (5) the average number of fetuses in each group. The last is important because Hammond shows that the number of fetuses in a uterine horn affects the amount of growth taking place in it.

Uterine Growth at Different Stages of Pregnancy.—With this information one may plot in a graph the weights of the products of conception (distention-mass) and the weights of the gravid uterine tissues on the different days of gestation.* Fig. 1 shows such a correlation. In addition to these two curves, the weights of the sterile horn equivalents are shown in Curve C.

In this graph, attention is called to two features in particular. In the first place, during the latter third of pregnancy in the rabbit, the

*Pregnancy in the rabbit lasts thirty-two days.

however, if the tension becomes too great the growth-response is affected adversely, especially in the endometrium, through impairment of the blood supply.

III. THE RÔLE OF UTERINE DISTENTION IN PREGNANT RABBITS

The physiologic significance of the facts described above is concerned with changes occurring during gestation since distention is an ever changing factor throughout most of pregnancy. Fortunately, suitable data on the growth of the uterus and of the products of conception are available in a recent paper by Professor Hammond, of Cambridge, in the Russian Journal, *Transactions on the Dynamics of Development*.³ The data given are for the rabbit, thus enabling one to make analysis of them directly from the standpoint of the distention-growth responses described above, which were likewise obtained in the rabbit. Markee, Wells and Hinsey⁷ have also published quantitative data on uterine growth during pregnancy in rabbits and these have been used to support Hammond's data.

Experimental Data Available for Study.—In Table I, I have modified some data from Tables I and VIII in the paper by Hammond. The changes made are first, to take the sum of the weights of the fetuses, fetal fluids, fetal placentas and membranes, and the maternal placentas. Values for these are given separately by Hammond for selected days of pregnancy. Since together they constitute the distention-mass in pregnancy, they have been grouped in the present paper under the term "distention-mass." The second modification of Hammond's data is found in the column headed "sterile horn mass." Hammond quotes weights (his Table VII) for a single sterile horn in unilateral pregnancies, while the weights of the gravid uteri are given in Table I for two uterine cornua. It is desirable to know what part of the

TABLE I. WEIGHTS OF THE REPRODUCTIVE ORGANS OF THE RABBIT AND OF THE PRODUCTS OF CONCEPTION AT DIFFERENT STAGES OF PREGNANCY
(FROM HAMMOND). SEE FIG. 1

DAYS OF PREGNANCY	AVERAGE NUMBER OF EMBRYOS	DISTENTION-MASS: PRODUCTS OF CONCEPTION	MASS OF THE GRAVID UTERINE TISSUES	MASS OF STERILE HORN EQUIVALENTS
		(GM.)	(GM.)	(GM.)
0	0.0	0	6.50	6.50
8	9.0	0.284	7.80	
12	9.7	2.673	15.54	
16	6.2	6.73	16.54	6.46
20	7.5	11.92	27.17	
24	5.2	28.35	35.68	15.00
29	4.7	52.01	32.61	16.90
30	5.3	58.11	37.05	17.68
32	4.8	75.44	48.81	20.58

gravid horn mass at each of the stages of pregnancy studied is equivalent to the sterile horn mass. This may be done by multiplying by

hormonic influence of estrin is becoming increasingly pronounced after the twentieth day. Other evidence dealing with the reactivity of the uterus at this time might also be adduced if other support for this conclusion were necessary.^{10, 11, 12} Parenthetically it may be noted that estrin is present in increasing amount in the blood and urine of the human being up to the time of parturition.²

This conclusion raises a point, however, which must be considered before any special significance may be attached to it. If one calculates the percentage increase in the mass of sterile horn equivalents on the different days of pregnancy over the mass of uterine tissues present at the start of pregnancy, he will find (as also shown in Fig. 1) that this increases from about day twenty until the end of gestation. This is shown by Curve B of Fig. 2. Since this growth of the sterile horn is attributable to hormone influences, as shown above, it is in all prob-

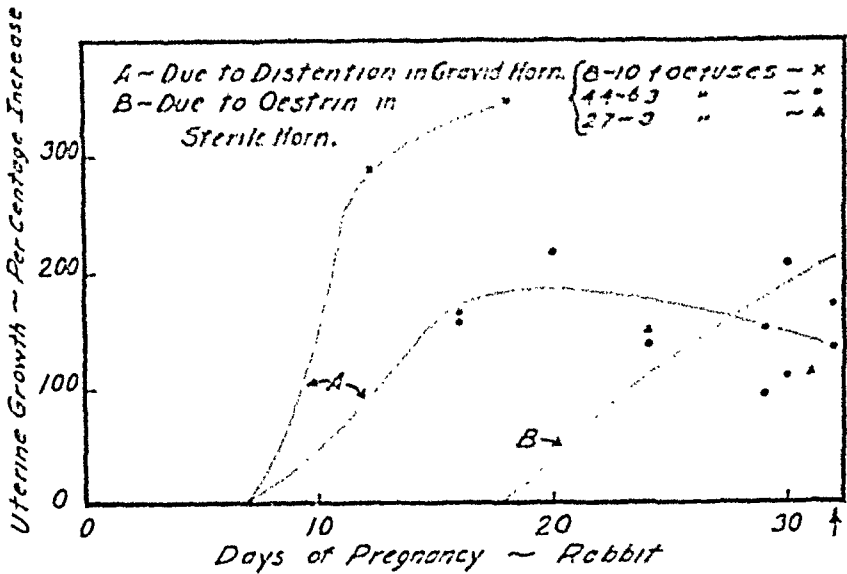


Fig. 2.—Chart showing the growth (percentage increase) during pregnancy of the gravid uterus (A), which is attributable to the distention-mass (products of conception), and the growth (percentage increase) of the sterile horn mass in unilateral pregnancies (B). See text for mode of calculation and significance.

ability associated with a rise of estrin which, as also pointed out above, is limiting the distention-growth response of the gravid uterus at this time.

IV. ESSENTIAL PHYSIOLOGIC CONDITIONS NECESSARY FOR THE ONSET OF LABOR

The important question arises, therefore: Does the uterine growth which is attributable to hormonal influences (specifically, estrin; Curve B, Fig. 2) after the twentieth day compensate for the diminishing influence of the distention-mass on uterine growth, shown in Curve A of Fig. 2? If it does compensate, then the uterus will continue to grow and in so doing will accommodate more readily the growing conception-mass; if not, it is inevitable that the disproportion between

rate of growth of the gravid uterus decreases whereas that of the products of conception increases to a maximum. Thus, from the twentieth day on, an increasing disproportion exists between the size of the distention-mass and the size of the uterus which surrounds it. In other words, the gravid uterus approaches the limit of its capacity to grow, for the conditions existing near the end of gestation. More will be said of this correlation below.

In the second place, Curve C shows that between the sixteenth and the twenty-fourth day, the sterile horn of a unilateral pregnancy commences to increase in size. Hammond points out that this takes place about the twentieth day. The second correlation to be noted, therefore, is that as the curve for the distended, gravid uterine horn (Curve B) becomes flattened, that for an undistended horn exposed to the same hormonal influences begins to increase (Curve C). These facts are elucidated still further by an analysis of the data in the manner employed in the pellet work described above. Such an analysis is made as follows.

Uterine Growth During Pregnancy Attributable to the Distention-Mass.—With Hammond's data arranged as in Table I, one may easily compute the percentage increase of the mass of the gravid horn (Curve B, Fig. 1) over the mass of the sterile horn equivalent (Curve C, Fig. 1) in each of the gravid horn-mass values for any day of pregnancy. This percentage increase represents, as in the pellet work described above, the amount of growth which is attributable to the distention-mass. This is so, since the sterile horn equivalent is comprised of the mass of tissue present at the outset of pregnancy, plus the increment resulting from growth due to hormonal influences. These values have been calculated and are indicated in Fig. 2.

In this graph it was necessary to treat the data according to the number of fetuses present, because, as Hammond observes, this affects the amount of uterine growth. Accordingly, what is shown in Curve A of Fig. 2 is a family of curves of varying magnitude but having similar contours. Taken together, they show that uterine growth which is attributable to the distention-mass increases up to the twentieth day, and after this time it decreases somewhat, as shown by the flattening of the curve. A similar curve has been obtained with the data of Markee, Wells and Hinsey.⁷

It may be noted in passing that the growth responses obtained up to about the twentieth day are compatible with the data obtained in the distention-growth work in progestin-treated rabbits, described above.

The fact that after the twentieth day the growth due to distention decreases, taken in consideration with the fact that estrin exerts an inhibiting effect upon the distention-growth response, shows that the

From this time on, the proportion of the gravid uterus which is attributable to hormone (estrin, see above) influences increases as the proportion due to distention becomes about constant, *pari passu*.

It is highly significant (and this is in answer to the question asked above) that at no time does the growth-increment which may be assigned to hormone influences equal the growth-increment which is attributable to the presence of the distention-mass. At most, according to these data, it exerts about half the effect that the distention-

TABLE II. PROPORTION OF GRAVID UTERINE TISSUES ATTRIBUTABLE (1) TO THE TISSUES PRESENT AT THE START OF PREGNANCY; (2) TO GROWTH RESULTING FROM HORMONE INFLUENCES; AND (3) TO GROWTH RESULTING FROM THE DISTENTION-MASS (PRODUCTS OF CONCEPTION).
BASED ON HAMMOND'S DATA FOR PREGNANCIES
WITH 4.7 TO 6.3 FETUSES. SEE FIG. 3

DAYS OF PREGNANCY	PER CENT ATTRIBUTABLE TO ORIGINAL TISSUES	PER CENT ATTRIBUTABLE TO HORMONE INFLUENCE	PER CENT ATTRIBUTABLE TO DISTENTION
0	100.0	0.0	0.0
16	39.3	0.0	60.7
24	18.2	23.8	58.0
29	19.9	31.9	48.2
30	17.6	33.8	48.6
32	13.3	28.9	57.8

mass factor does in uterine growth, in the latter part of pregnancy. Clearly, therefore, the reason why uterine growth at the end of gestation in the rabbit does not keep pace with that of the fetus and its associated parts is due, first, to the limiting action of estrin upon the distention-growth response of the uterus and, second, to the fact that estrin is relatively ineffective as a direct growth-promoting stimulus to the gravid uterus at this time. One must also conclude that the uterus has about reached its limit of capacity to grow at the end of gestation for the conditions obtaining at that time. New or different conditions conceivably may advance the time when the limit of uterine growth is obtained and result in abortion or premature delivery, or they may retard it and give rise to prolongation of pregnancy.

The above conclusion depends upon the assumption that the gravid uterine tissues utilize the available hormones to the same extent as do the uterine tissues in the sterile horn of a unilateral pregnancy. This may or may not be true, however. If the gravid tissues utilize the available hormones to a less extent than do the sterile horn tissues, then the cogency of the argument advanced above is enhanced because the reduced growth-promoting effect of distention after the twentieth day would be proportionately greater. On the other hand, the gravid tissues may grow relatively more because of the hormone; even so the growth which takes place is still insufficient to prevent the increasing disproportion in the growth rates of the uterus and of the products of conception, as shown by Curves A and B in Fig. 1. The main conclusions derived from the foregoing considerations are essentially valid, therefore.

the growth of the uterus and the growth of the fetus (shown in Fig. 1) will result in a gradual but ever increasing intrauterine tension. This condition in association with the fact that estrin increases rhythmic uterine contractility⁸ would result in a condition which is incompatible with retention of the uterine contents. Moreover, the increasing tension on the uterine wall would improve, up to a certain point, the efficiency and forcefulness of the developing uterine contractions.

If the answer to this question is known, therefore, it may be possible to regard the conditions leading up to the onset of labor as a gradual, accelerating convergence of a number of influences, hormonal, nutritional and physical, which must in the normal course of events result in evacuation of the uterus. Fortunately, it is possible to supply the answer to this question with data given in Table I. This is done in the following manner:

Hammond's data show that during the first week of gestation in the rabbit, no appreciable increase in the size of the uterus occurs (Curve B, Fig. 1); the growth at this time is almost entirely that of

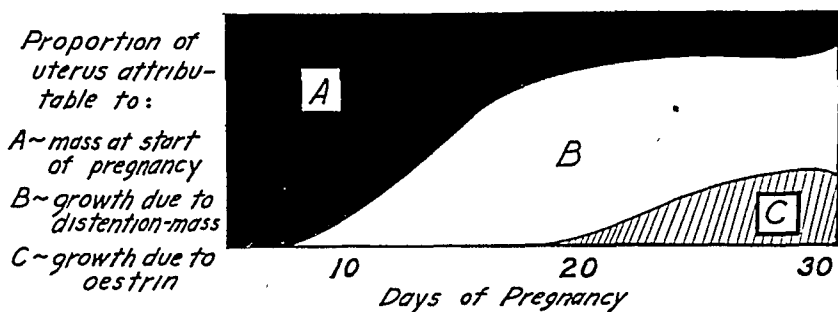


Fig. 3.—Chart showing for each phase of pregnancy the proportion of the gravid uterus which is attributable to the tissues present at the start of pregnancy (A), to the growth-increment attributable to the distention-mass (B), and to the growth increment attributable to the action of estrin (C). See text.

progressive differentiation of certain tissues. Between the eighth and twelfth days (by which time the ova have become attached and commence to grow rapidly) definite uterine enlargement begins. The problem that must be solved is to ascertain at the several stages of pregnancy (16, 24, 29, 30, 32 days) that part of the gravid uterine mass (taken as 100 per cent) which accounts for the tissues present at the start of pregnancy; that proportion which accounts for the growth-increment resulting from the presence of the products of conception, and that proportion which accounts for the growth-increment due to hormonal influences. This has been done and the values are given in Table II. Fig. 3 is based on these calculations from Hammond's data obtained from rabbits having an average of 4.7 to 6.2 fetuses each.

This chart shows that until about the eighteenth day, uterine enlargement takes place almost entirely as a result of the presence of the distention-mass as allowed (or favored) by the action of progestin.

untreated, ovariectomized rabbits and in rabbits under the influence of progestin. When estrin is the predominant hormone, the capacity of the distended uterus to grow is appreciably reduced.

With these facts as a basis, analysis is made of Hammond's data on uterine and fetal weights at different stages of gestation in the rabbit. It is shown that a disproportion exists between the growth increments of the fetuses and of the uterus in the last third of pregnancy, the former growing much more rapidly than the latter. It is further shown that the reason for the increasing disproportion of these growth rates is due largely if not entirely to an increase in the influence of the hormone, estrin. Mention is also made of the fact that estrin is the hormone demonstrated to have the property of imparting rhythmic contractility to the uterus. As a consequence of the limitation of the capacity of the uterus to grow, along with the continued increase in the size of its contents, it is pointed out that the developing rhythmic uterine contractions are rendered increasingly more efficient and forceful. The theory is advanced, therefore, that these physiologic conditions are the underlying factors which are essential to the onset of labor, and the commencement of parturition is the result of a gradual and accelerating convergence of these factors, bringing about nutritional changes and an appropriate physical orientation of the fetuses. Finally, the common physiologic basis between these conditions favoring the onset of labor and those which may be responsible for spontaneous abortion is discussed.

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It is clear from the foregoing considerations that the theory advanced in the sequel to the question stated above has an experimental basis of fact. It is to be emphasized, however, that this theory is not all-exclusive, for it does not preclude the probability of a multiplicity of other factors also being concerned in the normal termination of pregnancy. The theory has merit, however, since it defines in quantitative terms for the rabbit a number of growth-promoting factors and growth-limiting factors, the proper association of which must be achieved if labor is to begin.* In addition, emphasis has been laid upon the fact that the immediate cause of the limitation of uterine growth at this time (estrin) is also the stimulus for rhythmic uterine contractility which develops concurrently with the growth changes described above. By virtue of the combined effects of these conditions a means is thereby provided by which the developing rhythmic contractions of the uterus are rendered physiologically more effective for the expulsive functions they ultimately subserve at the time of parturition.

V. SPONTANEOUS ABORTION IN RELATION TO THE ONSET OF LABOR

To say that this theory provides a basis upon which the mechanisms associated with spontaneous abortion may be explained goes beyond the established facts. There are, however, several features in common between this condition and those described above which are necessary for the onset of labor. Chief among these is the fact that spontaneous abortion in the human is preceded for some time by an abnormal rise in the blood and urine levels of estrin.⁴ The presence of this hormone must necessarily preclude further uterine growth resulting from distention, on the basis of what has been said above. Such a condition is, as we have seen, one of major importance in determining the capacity of the uterus to accommodate the ovum. Clearly, therefore, increased intrauterine tension will develop and this will lead to death of the fetus through impoverishment of its nutritional supply, owing to interference with the vascular bed of the placenta. In the absence of additional facts it is unwise to speculate further in this connection. Enough information is available, however, to indicate that the conditions leading to spontaneous abortion may have a physiologic basis akin to those which lead to labor.

SUMMARY

At the outset, a review of the local physiologic effects of chronic uterine distention under various hormone conditions is given. It is shown that uterine growth resulting from distention takes place in

*In mammals with the so-called *uterus simplex*, orientation of the physical aspects of parturition would be relatively more important than in the rabbit, which has a bicornuate uterus. See (8) for discussion of the physical changes that must take place.

corticotropic. Thus to a certain extent the follicle hormone produces a biologic partial resection of the anterior lobe of the pituitary. Analysis of the pituitary of dwarf rats has shown that the content of gonadotropic hormone is not less than those of controls. From that it follows that it is not the production of gonadotropic hormone that is checked by follicle hormone, but only the delivery of the produced hormone into the blood stream. Follicle hormone then, causes a partial blockade of the anterior lobe of the pituitary. If this treatment with follicle hormone is continued for seven months, we note an interesting result. The pituitary changes into a tumor which can attain a size twenty-five times that of normal. The animals die with symptoms of intracranial pressure. So far I have been able to produce eighteen such tumors of the pituitary which I shall report in detail elsewhere.

In the present study, we are dealing with the effect of chronic treatment with hormone on the uterus. This effect is not a central one as the result of the inhibition of the pituitary, but the expression of a local effect of follicle hormone on the uterus itself. I feel particularly honored to contribute the results of this investigation to the volume dedicated to Dr. Robert T. Frank, to whom we are indebted for so many significant researches in the field of the follicle hormone.

In these experiments the rats received for a number of weeks doses of 5,000 M.U. dimenformon twice a week. It must be made clear that these are enormous, totally unphysiologic doses. But if we can attain definite reactions in the uterus, certain conclusions in reference to pathology are justifiable by analogy, for the ovary may produce very large unphysiologic amounts of follicle hormone for considerable periods of time, for instance, in certain disturbances which I have described under the heading of polyhormonal syndromes.² The best known of these is glandular cystic hyperplasia of the endometrium. It will be shown below that by chronic treatment with follicle hormone the endometrium may be destroyed and the uterus disintegrated by suppuration.

Partial inhibition of the anterior lobe function can be accomplished regularly by follicle hormone; in 140 test rats there was not a single failure. In the case of the uterus the situation is entirely different.* Under the same experimental conditions there may be no effect on the uterus of one rat and a high grade disturbance of the uterus of another. The uteri of various animals react differently; a fact which I report, but cannot explain. Space prevents me from describing the individual experiments, and I will, therefore, simply mention the quite characteristic changes. In practically all the experiments there was an extensive leucocytic infiltration of the mucosa particularly a subepithelial

*I should like to thank Dr. Joel and Dr. Karplus for their invaluable assistance in this work.

THE EFFECT OF LONG-CONTINUED LARGE DOSES OF FOLLICLE HORMONE UPON THE UTERUS OF THE RAT

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AS I have shown in previous studies, it is possible to eliminate certain functions of the anterior lobe of the pituitary by long-continued treatment with follicle hormone. If one treats young rats for a number of weeks with dimenformon (estradiolbenzoate), the following symptoms appear: the growth of the sexual organs ceases so that the scrotum disappears entirely, the testicles are no longer palpable, and the penis becomes small. After several weeks the difference between the weight of the testicles and those of the controls amounts to 95 per cent. Spermatogenesis disappears. The ovaries become so small that they are hardly visible to the naked eye. In serial sections occasional enlarged follicles are seen, never a corpus luteum. The same changes can be effected in birds. The cockcomb disappears, the testicles remain atrophic, and spermatogenesis ceases entirely. Secondly, disturbances of growth appear. The rats and fowl are retarded in growth, finally all growth disappears so that, for example, the subjects of the experiment are 26 per cent smaller and 60 per cent lighter than the controls. It is possible, then, by chronic treatment with follicle hormone to raise eunuchoid dwarf rats and dwarf fowl. The dwarfism is proportional, the head is smaller, narrower, the breast circumference less, the tail shorter, the internal organs and bones smaller and lighter. Characteristic changes of the bones are easily recognizable in the x-ray picture. (I described these elsewhere in detail.¹) The above-named effects are ascribable to the elimination of the influence of the secretion of the anterior lobe of the pituitary by the chronic treatment with follicle hormone, specifically the growth hormone and the gonadotropic hormone. That it is really the elimination of these hormones is evidenced by the fact that one can again stimulate growth of these dwarf rats by the exhibition of Evans' growth hormone. To a certain extent the atrophy of the genitals also may be halted by the simultaneous treatment with dimenformon-gonadotropic hormone. In this case, only the growth of the animal is disturbed and dwarfs with normal genitalia are produced.

Follicle hormone only eliminates certain functions. The thyreotropic and parathyreotropic hormones are not influenced, probably also not the

may be entirely missing while at the same time the contiguous site may show a stratified cylindrical epithelium with papillae and hydropic cells.

So far we have shown that the uterine mucosa after chronic treatment with follicle hormone shows typical changes, to wit: localized

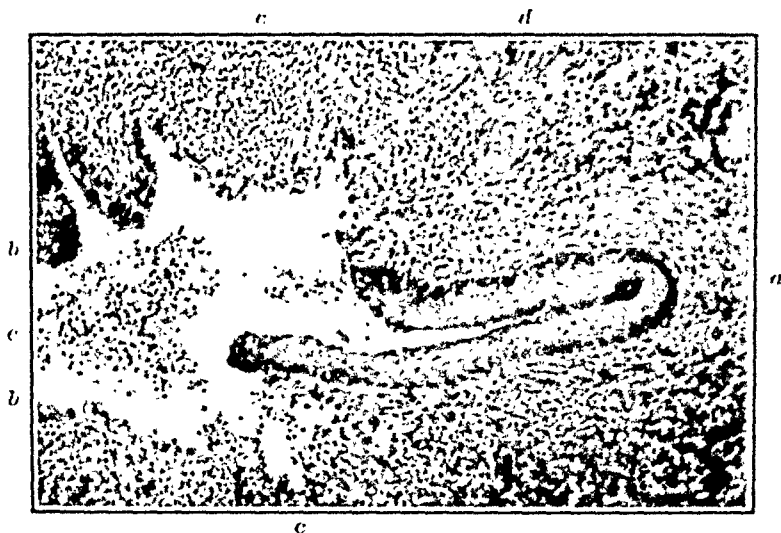


Fig. 3.—100 magnifications. Partial metaplasia of the uterine mucosa (*a*). One of the areas which is not metaplastically changed, shows only a single layer of epithelium (*b*). A massive leucocytic migration into the lumen (*c*). Gland lined with cylindrical epithelium (*d*).

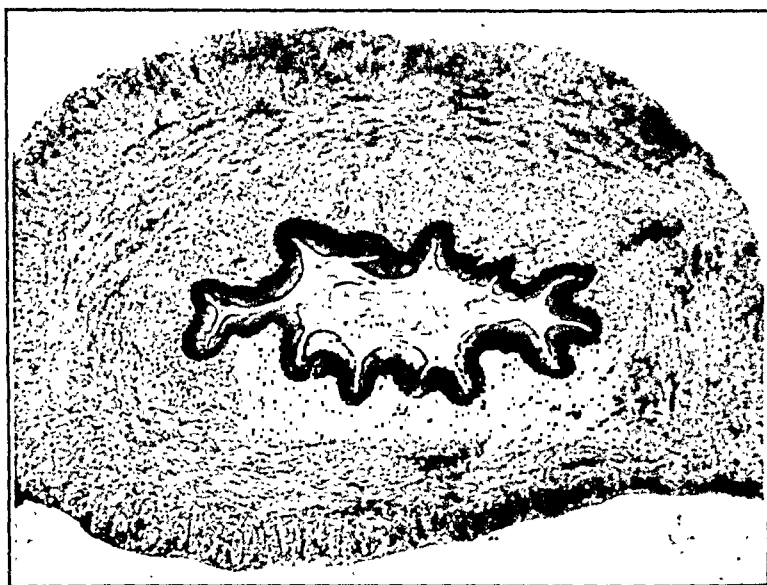


Fig. 4.—Cross-section of the uterus, 36 magnifications. Total metaplasia of the mucosa with stratified squamous keratinized epithelium, the uterus having the appearance of a vagina in estrus.

absence of epithelium, next to normal epithelium, as well as stratified cylindrical epithelium and papillary projections into the lumen of edematous high cylindrical cells, subepithelial leucocytic infiltration (eosinophiles) with transmigration into the lumen. It is of particu-

wall of eosinophiles, some of which wandered in numbers into the uterine cavity. I emphasize this because I believe that an inflammatory factor plays a considerable rôle in the changes described. It is characteristic that the epithelium can show considerable variation in the same section. There are stretches of normal single layered cylindrical epithelium; else-

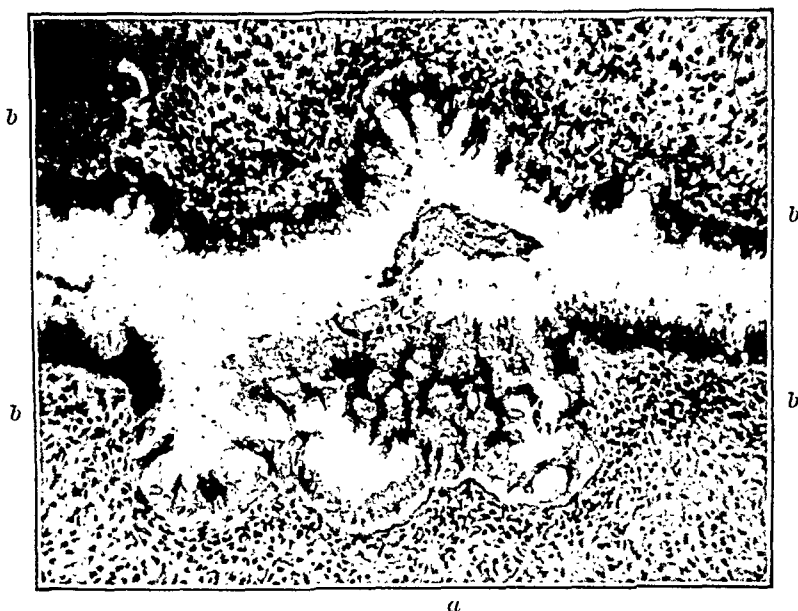


Fig. 1.—Cross-section of the uterus, 150 magnifications. The mucosa lifted off in areas. Hydropic cells without visible cell borders (*a*). An encircling ring of sub-epithelial eosinophiles (*b*). Some transmigration into the lumen.

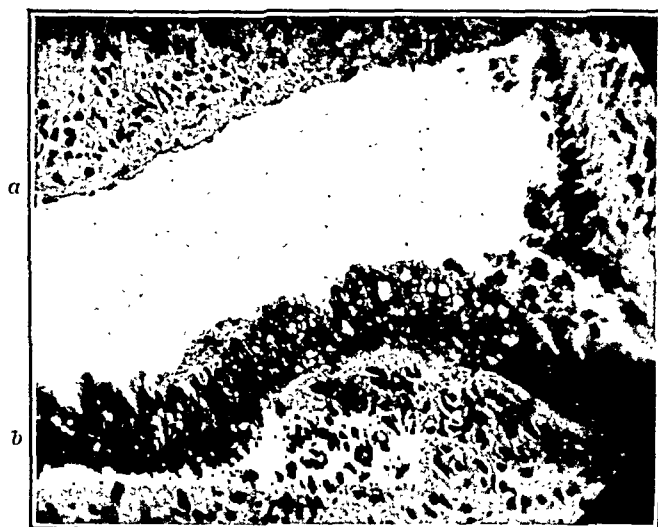


Fig. 2.—Cross-section of the uterus, 270 magnifications. Areas of absence of the surface epithelium (*a*) opposite to which there is a many-layered cylindrical epithelium with a suggestion of tufting and papillary formation and hydropic cells (*b*). Leucocytic infiltration of the mucosa.

where stratified cylindrical epithelium, often showing a tufted and papillary formation. The mucosa in certain portions is desquamated so that peculiar cell groups are found in the lumen; these contain hydropic cells without visible cell borders. In certain areas the surface epithelium

plasia of the uterine mucosa, the lumen lined by a stratified keratinized squamous epithelium, so that the uterus resembles a vagina in estrus. As in the case of the estral vagina, horny lamellae are shed into the lumen, the uterine cavity here is filled with them. The higher magnification of Fig. 5 shows this plainly. Here we also see a gland in the depth of the mucosa metaplastically altered into squamous epithelium, with prickle cells and intercellular bridges, the latter most plainly seen in Fig. 6, from another experiment. In Fig. 6 we note as well the metaplasia of the mucosa with flattened keratinized squamous epithelium. Just under the mucosa there is a gland lined by metaplastic



Fig. 7.—Cross-section of a uterus, 150 magnifications. Mucosa varies in composition. At (a) stratified cylindrical epithelium. At (b) papillary projections into the lumen of edematous high cylindrical cells. At (c) complete absence of epithelium. At this point a polyp of uncornified stratified epithelium projects into the lumen (d). Subepithelial gland lumen filled with metaplastic stratified epithelium.

squamous epithelium in which the prickle cells and intercellular bridges can be recognized. The last stage is the complete suppuration of the uterus, changing it into a sac the thickness of a thumb, filled with pus (Fig. 9). The cavity of the uterus is enormously dilated (Fig. 8) contains desquamated horny lamellae, cell detritus, and pus. The mucosa of the uterus shows a circular purulent liquefaction and contains numerous abscesses. In part the continuity is interrupted and is held together by the serosa alone. Those portions of the muscularis which have fallen victim to the suppuration show heaps of pseudoxanthoma

lar interest that the uterine epithelium can undergo a complete metaplasia under the influence of follicle hormone so that at first glance the uterus may appear like the vagina in estrus. Fig. 3 shows a partial metaplasia of the uterine mucosa in which we see leucocytes in the lumen and a metaplastic mucosa protruding into the lumen. The leuco-



Fig. 5.—Same as Fig. 4, magnified 150 times. Oil immersion. Section of the totally metaplastic uterine mucosa. Horny lamellae extruded into the lumen. In addition there is a metaplasia of a gland lining (*a*).

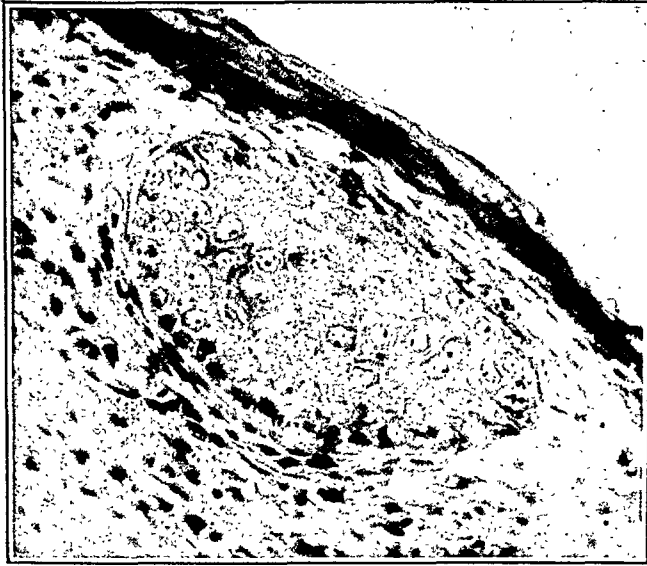


Fig. 6.—400 magnifications. Oil immersion. Metaplasia of uterine mucosa. Flattened horny stratified epithelium. In the mucosa a gland completely filled with metaplastic stratified epithelium showing prickle cells and intercellular bridges.

cytes reach the horny layer. That portion of the mucosa which is not metaplastic shows a single layer (Fig. 3, *b*) of epithelium not the normal cylindrical. In the stroma there is a gland lined by squamous rather than cylindrical cells (Fig. 3, *d*). The whole mucosa shows a thick leucocytic infiltration predominantly eosinophilic, as well as a perivascular infiltration of the muscularis. Fig. 4 shows a complete meta-

cells (Fig. 8, *a*), which determine the macroscopic yellow color of the uterine horns. We are evidently dealing with a long-standing process. We were able to observe the suppuration clinically in various stages and it could be diagnosed by the appearance of pus in the vagina. In some cases the uterus seemed barely enlarged (the thickness of a slate pencil), nevertheless on section creamy pus was found in the lumen. In other cases the pus sacs were tremendous as, for instance, in Fig. 9. Some of the animals died of peritonitis. Bacteriologic investigation of the uterine secretion showed gram-positive diplococci and bacilli, gram-negative bacilli, and occasional fusiform bacilli.

In brief, then, it is evident that as a result of chronic treatment with follicle hormone the following changes are seen in the uterus of the rat: multilayered cylindrical epithelium with polypoid formation, focal absence of the surface epithelium, focal desquamation of areas of mucosa with hydropic cells without visible cell boundaries, partial to total metaplasia of the uterine mucosa with discharge of horny lamellae into the lumen, metaplastic alteration of the glands, stratified epithelium, leucocytic infiltration of the mucosa with transmigration of leucocytes into the uterine cavity, pyometra with abscess formation of the musculature, and consequent exitus.

In an earlier study³ I have described the effect of chronic treatment with follicle hormone on the uteri of rabbits in which four characteristic reactions were determined:

- A. Hyperemia of the endometrium and musculature and occasional small mucosal hemorrhages
- B. Glandular cystic hyperplasia of the endometrium
- C. Infaretlike necrosis of the endometrium
- D. Aseptic suppuration of the uterine cavity

The glandular cystic hyperplasia is caused by a direct action of follicle hormone on the endometrium. The other reactions are the result of thromboses. There is a consequent infaretlike necrosis and secondary to this, an aseptic suppuration of the uterine cavity. In the case of the rat the leucocytic infiltration appears very early so that it is not surprising that there is ultimately a partial infection, complete suppuration and disintegration of the uterus. I have not noted metaplastic changes of the mucosa and of the glands in rabbits nor have I seen thromboses and infaretlike necrosis in rats. Hence, we can deduce that the uteri of rats and rabbits react differently to treatment with follicle hormone. When I stated in the above-quoted study that chronic treatment with follicle hormone evoked no determinable changes in the uterus, I was wrong. I had treated rats and rabbits for the same length of time and saw no effect on the rats, but by continuing the treatment of the rats one can obtain the reaction that I have described today.

Selye, Thomson and Collip⁴ report that they have obtained a beginning metaplasia of the uterine mucosa in three cases and a complete



Fig. 8.—Cross-section through the uterus, 9 magnifications. Uterine cavity widely dilated, in the lumen there is pus and detritus. Uterine wall is studded with abscesses some of which reach the serosa. At various points, heaps of pseudoxanthoma cells (*a*).

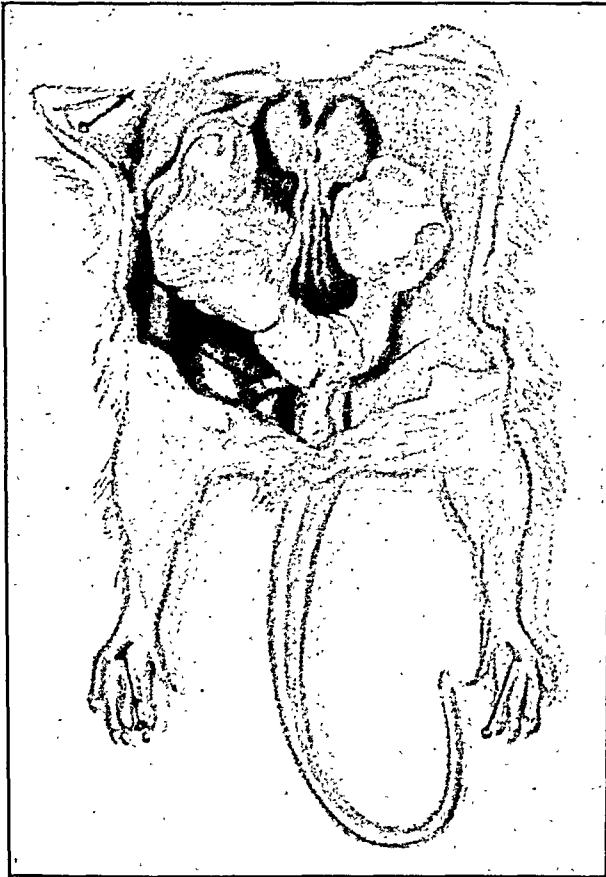


Fig. 9.—Uterus of a rat after eight months' treatment with estrogenic hormone (dimenformon). Both horns converted into huge pus sacs.

B. Partial to total metaplasia of the surface epithelium into stratified keratinized squamous epithelium, the uterus having the appearance of a vagina in estrus.

2. *Metaplasia of the glands*, change of the normal glandular epithelium into squamous epithelium with prickly cells and intercellular bridges.

3. *Inflammatory changes*, leucocytic infiltration of the entire mucosa, a sub-epithelial wall of eosinophiles, transmigration of leucocytes into the uterine cavity, suppuration of the mucosa (pyometra) and destruction of the musculature with conversion of the uterine horns into pus sacs of the thickness of a thumb.

Suppuration of the uterus also occurs in rabbits as a result of long-continued treatment with follicle hormone. This suppuration is aseptic and occurs after thrombosis and resultant necrosis. In contrast to this there is a secondary infection in the case of the rat. The ovaries of the experimental animals show a high grade atrophy, occasional enlarged follicle, never a corpus luteum.

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metaplasia in one case by treating castrated rats with follicle hormone after previous ligation of the uterine horns. We have here the combined action of a mechanical irritant and a hormonal one, reminding us of the well-known researches on experimental placentomas (Gloeb, Calderini, Long and Evans and others). In my own investigations, on the contrary, we are dealing with effects produced by hormones alone.

After my work was completed there appeared the publications of Gumbrecht⁵ and Migliavacca⁶ who also describe metaplastic changes in the mucosa as a result of long-continued treatment with follicle hormones. Migliavacca in a very interesting study shows that plugs of squamous epithelium project deep into the wall of the uterus up to the smooth musculature. He describes, in addition, considerable invasion of the myometrium by these projections and discusses the question of a precancerous lesion. From my own investigations I have never had the impression that we were dealing with a process which could in any sense be designated as malignant. We cannot conclude from the above reactions that malignant tumor formation can be produced by treatment with follicle hormone. Although Migliavacca used some non-castrated animals, most of his experiments were on castrated animals. After castration prolactin A is produced in increased quantity by the pituitary, so that castrated animals in whom one injects follicle hormone over a long period are under the influence of two hormones, both prolactin A and follicle hormone. Perhaps this plays a rôle in the experiments of Migliavacca. In any event I should like to emphasize that even after seven months of treatment of rats with enormous doses of estrogenic hormone (1,080,000 M.U. dimenformon) I have never seen pictures which one could interpret as malignant tumors or precancerous lesions, if such exist. It may be mentioned that Migliavacca in a previous study⁷ has described changes in the mucosa such as reduplication of layers, vacuolization, hydropic degeneration as a result of long-continued treatment with follicle hormone.

CONCLUSIONS

The effect of long-continued treatment with follicle hormone on the uterus in the rat is described. Though the inhibitory effect upon the anterior lobe of the pituitary by follicle hormone, expressed in eunuchoid dwarfism, appears uniformly in all the animals, the local effect on the uterus itself varies widely. Sometimes there is no effect, sometimes a complete destruction of the uterus. The effect of the estrogenic hormone therefore varies individually. The following characteristic effects were established:

1. Effects on the Epithelium.—A. Marked variability, focal absence of the epithelium, stratified cylindrical epithelium, tufts and papillae projecting into the lumen, desquamation of whole areas of the mucosa, with hydropic cells without visible cell boundaries.

The fact that so many more Aschheim-Zondek tests than Friedman tests are carried out demands an explanation. The Friedman test must necessarily be more expensive than the Aschheim-Zondek; rabbits are more difficult to breed, to procure, and to accommodate in large numbers

TABLE 1

			POSITIVE	NEGATIVE	UNFINISHED	DISAGREEMENT	CONFIRMED AS CORRECT
For ordinary pregnancy diagnosis	Aschheim-Zondek	6537	3415	3092	30	—	2001
	Friedman and confirm. A-Z.	388	197	173	1	23	201
	Friedman alone	83	42	38	3	—	33
		7008	3654	3303	34	17	2235
							MODIFIED A-Z
For detection of hydatidiform mole, chorionepithelioma, or recurrence of these							171
For detection of malignant tumor of the testis in the male							14
For quantitative estimation of sex hormones							13

than are immature mice; the adult rabbits which are used in this Laboratory require to be isolated for at least four and a half weeks before use; an injection into a rabbit's ear-vein requires more skill than does a subcutaneous injection in the mouse; and, finally, it is very difficult in our experience to purchase rabbits free from disease. It would appear, moreover, that in the majority of cases in which the help of this Laboratory is sought, urgency is not a serious consideration: a report after five days is quite sufficient. Analysis of the records shows that the Friedman test is required mainly in those cases in which the size of the fee has not to be considered; in which urgency exists: e.g. in the differential diagnosis of ectopic gestation; in cases in which, if pregnancy exists, it must be terminated for medical reasons; and in cases in which the information sought is urgently desired for the reason that, if pregnancy is shown to exist, certain domestic arrangements must be disturbed. The Laboratory offers a choice of tests; it is the practitioner who decides. The great preponderance of the Aschheim-Zondek in our records has always been a matter of surprise to me, for I had assumed that the rapid test would be the one in greater demand. However, I am very content that the demand is mainly for the slower Aschheim-Zondek, for though the Friedman in our hands is undoubtedly the more delicate of the two, the Aschheim-Zondek is the more convenient procedure when very many tests are being carried out every day, and moreover, the graded reactions that are obtained therein provide the means of distinguishing between several relative concentrations of the gonadotropic hormones in different specimens, and permit us to refer a strong positive, a rather weak positive, a weak positive, an extremely weak positive, a negative with uterine and

NOTES FROM A PREGNANCY DIAGNOSIS LABORATORY (1936)

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THE state, concerned with the problems that must arise out of the dwindling of a population, a change in the mean age, and a swing in the sex ratio, is demanding knowledge of the biologic as well as of the economic factors that influence the wish and the ability of individuals to reproduce. Society demands that medicine shall gain control of those wasteful derangements peculiar to women, and shall rid childbearing of baseless dread and preventable danger. Medicine is responding. The search for new knowledge concerning human sex and reproductive physiology is eager, and the application of biologic science to human affairs follows immediately upon discovery. It is in this field of enquiry that intellectual adventure is to be most readily encountered, and that kind of immortality which a scientist hopes to achieve is to be earned. Among those whose names will certainly be respectfully and gratefully remembered in the history of this branch of medicine is that of the man to whom this volume is a memorial. We who write have shared his joy in his discoveries, and we gladly pay tribute to the quality of the man and of his work. To him this Laboratory is greatly and continually indebted; upon his knowledge and wisdom it has frequently relied.

Among the instruments of precision that medicine has devised and used in the execution of its purposes and ideals, there is none finer than the biologic test for early pregnancy. Its value to the profession, to the general public, and to the state is amply illustrated in this Report of a Pregnancy Diagnosis Laboratory which was organized some six years ago in order to place the then-new exploitation of scientific discovery at the service of the medical profession of Great Britain. It was thought then (and nothing has occurred since to disturb this view) that a specialized laboratory with its own breeding plant, its duplicated and highly-skilled staff, and operating on a large scale, could best give an adequate service with graded fees that would make the tests available for all, irrespective of income category, and, at the same time, accumulate data sufficient for profitable analysis.

In 1936, 7,193 specimens were examined. Of these, 3,791 fell into the "full-fee" class, while 3,402 came from patients in poor circumstances who were asked to pay according to their means.

The tests were distributed as shown in Table I.

conception had occurred twelve days, and in another fourteen days, before the specimen was taken. In yet another, in which it was known that pregnancy was of very short duration, if it existed at all, the test, repeated ten days later, gave a positive reaction. Experience has shown that too much reliance cannot be placed upon a negative Aschheim-Zondek result in the case of a patient less than one month pregnant. In 11 of the remaining cases the duration of pregnancy had been longer, four weeks in 1 case, seven weeks in 1, eight weeks in 2, fourteen weeks in 2, sixteen weeks in 1, nineteen weeks in 1, and twenty-four weeks in 3. One false negative was obtained in a six weeks' pregnancy that ended in abortion, and another related to a case of pregnancy in a woman suffering from Graves' disease. This case was of particular interest, and the patient was followed throughout pregnancy. At the second month the Aschheim-Zondek test was negative, at the fourth month positive, at the fifth month negative, and at the seventh positive (weak) again.

Of the five false positives, two are without any explanation. The doctor in charge of one case, on clinical grounds, had reason to doubt the correctness of this result. The test was repeated one month later to give a straight forward negative test. In the other, the patient had left the district and nothing was known of her subsequent history. In the remaining three cases, a weak positive result was recorded (faint blood spots and white spots in two mice only). In one of these the patient was suffering from "congestive heart disease"; in another, she had been receiving treatment for "thyroid and pituitary disturbance," and the third, suffering from hemorrhage, had been curetted.

In addition to these errors, a number of unclear results were obtained in the case of specimens derived from single women greatly fearing pregnancy. Two factors undoubtedly affected the value of the reports issued in these cases. In the first place it seems clear that the emotional condition of the patient can have endocrine repercussions which can affect the reaction of the mice, and second, in the case of patients by whom pregnancy is feared, the incorrectness of a positive result strongly suggests that abortion has taken place. When the history supports this explanation, the result is not regarded as incorrect.

As in previous years, the errors are found to be concentrated at the beginning and at the end of the reproductive phase of life. The young unmarried girl aged thirteen to seventeen years, and the woman of forty-three plus, are very unsatisfactory in respect of these biologic tests for early pregnancy.

NEGATIVE ASCHHEIM-ZONDEK RESULTS—REPETITION ADVISED

In no less than 573 cases in which a negative Aschheim-Zondek result was recorded, it was necessary (for the reason that though the ovaries of the mice remained unaffected, their uteri and vaginae were much enlarged) to send with the report a slip intimating that though according

vaginal enlargement to a variety of different conditions. Thus, a weak positive following upon a succession of strong positives in a case of habitual abortion permits us to warn the doctor that all may not be well. A weak positive in a case in which abortion is suspected to have occurred provides support for this diagnosis. A negative with vaginal and uterine enlargement at once raises the question as to the age of the patient.

The Friedman test is always used in cases in which medicolegal interest is concerned and is followed up by an Aschheim-Zondek. In such cases a preliminary laparotomy is performed on two rabbits, and their ovaries are examined to ensure that ovulation has not recently occurred. Ten cubic centimeters of filtered urine is then injected into the ear-vein of each. Thirty hours later one rabbit is killed. If it shows a positive result, the second rabbit is returned to store, if negative, a further 10 c.c. is injected into the second rabbit, and this animal is killed thirty hours later. If this one also gives a negative, this result is regarded as trustworthy.

The combined Friedman and Aschheim-Zondek is the test that is to be preferred in the case of suspected ectopic gestation. The information that these tests give in such cases has proved time after time to be of the greatest possible value.

Specimens from a series of cases of ectopic gestation operated upon in the Royal Infirmary of Edinburgh were examined. Specimens from 14 cases taken within eight hours after the operation, and thereafter daily for seven days, were tested, and in every case a definite negative test was invariably obtained seventy-two hours after the removal of the embryo. To the surgical and nursing staff of the Wards concerned, I wish to offer my thanks.

In a very considerable number of cases, the question of fetal death was raised. In these cases the tests have not proved to be entirely satisfactory. It is true that commonly the "strength" of the reactions on the part of rabbit and mouse have been such as to indicate a relatively low concentration of gonadotropic hormones and thus support the tentative diagnosis. Indeed, definite negatives are not uncommon. But in other cases quite strong positives have been obtained as long as a month after the time when, according to the clinical evidence, the fetus had perished. However, for the present, the combined Friedman and Aschheim-Zondek is the most useful test in these cases. The quantitative blood estrin test does not appeal to the general practitioner, for the obvious reason that it is far easier to obtain a specimen of urine than one of blood.

ERRORS

In the Aschheim-Zondek Tests: 16 false negatives, and 5 false positives.

Three of these false negatives are to be explained by the fact that conception had too recently taken place. In one case it was known that